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L21 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:405429 HCAPLUS

DOCUMENT NUMBER: 142:435832

TITLE: Pharmaceutical formulations for carrier-mediated transport statins and uses thereof

INVENTOR(S): Butler, Jackie; Devane, John; Stark, Paul

PATENT ASSIGNEE(S): Athpharma Limited, Ire.

SOURCE: PCT Int. Appl., 80 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005041939	A1	20050512	WO 2004-IB3849	20041029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005119331	A1	20050602	US 2004-967167	20041019
PRIORITY APPLN. INFO.:			US 2003-516770P	P
				20031104
			US 2004-967167	A
				20041019

AB The present invention relates to formulations comprising therapeutically effective amts. of at least one acid-stable,

carrier-mediated transport statin, at least one poorly water-sol., carrier-mediated transport statin, or at least one large mol. wt., carrier-mediated transport statin, such as atorvastatin and rosuvastatin, or a pharmaceutically acceptable salt thereof, and methods of their use. The present formulations and methods are designed to exhibit a controlled-release of a therapeutic amt. of the statin in the small **intestine**, thereby limiting systemic exposure of the statin and maximizing liver-specific absorption of the drug. The formulations and methods of the present invention are particularly useful for treating and/or preventing conditions that are benefited by decreasing levels of lipids and/or cholesterol in the body. Modified-release compressed tablets contained atorvastatin 5.00, lactose 45.58, Avicell PH101 28.72, Methocel K100LV 20.00, colloidal silicon dioxide 0.20, and magnesium stearate 0.50%.

IC ICM A61K009-20

ICS A61K009-28; A61K031-40; A61K031-505; A61P003-06

CC 63-6 (Pharmaceuticals)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN  
THE RE FORMAT

L21 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:259869 HCAPLUS

DOCUMENT NUMBER: 142:322767

TITLE: Treatment of gastroparesis and nonulcer  
dyspepsia with gabab agonists

INVENTOR(S): Devane, John; Butler, Jackie

PATENT ASSIGNEE(S): AGI Therapeutics Ltd., Ire.

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005025559	A1	20050324	WO 2004-IB3299	

200409

10

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA,  
CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,  
KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,  
SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,

VC, VN, YU, ZA, ZM, ZW  
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,  
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,  
DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL,  
PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
GW, ML, MR, NE, SN, TD, TG

US 2005090554

A1

20050428

US 2004-935176

200409  
08

PRIORITY APPLN. INFO.:

US 2003-502242P

P

200309  
12

US 2004-553940P

P

200403  
18

AB The present invention relates to formulations comprising a therapeutically effective amt. of baclofen or (R)-baclofen, or pharmaceutically acceptable salts thereof, and methods of their use. The present formulations and methods are designed to release a therapeutic amt. of baclofen in a manner that maximizes its therapeutic effect. The methods and formulations are esp. suitable for treating gastroparesis and nonulcer dyspepsia. A modified-release tablet contained (R)-baclofen 2.5, lactose 20.58, microcryst. cellulose 51.22, Methocel 20.00, colloidal silicon dioxide 0.20, magnesium stearate 0.50, and PVP 5.0%. Pharmacokinetics of the tablets were studied in healthy volunteers.

IC ICM A61K031-195

ICS A61K009-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

IT **Intestine**

(small; treatment of gastroparesis and nonulcer dyspepsia with gaba agonists)

IT Amyloidosis

Diabetes mellitus

Drug delivery systems

Gastric emptying

**Gastrointestinal motility**

Human

Hypothyroidism

Parkinson's disease

(treatment of gastroparesis and nonulcer dyspepsia with gaba agonists)

REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN  
THE RE FORMAT

L21 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2005:216689 HCAPLUS  
DOCUMENT NUMBER: 142:285208  
TITLE: Controlled-release formulations of  
aminosalicylates for treating inflammatory  
bowel disease  
INVENTOR(S): Devane, John; Butler, Jackie  
PATENT ASSIGNEE(S): AGI Therapeutics Ltd., Ire.  
SOURCE: PCT Int. Appl., 96 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005021009	A2	20050310	WO 2004-IB3059	20040902
WO 2005021009	A3	20050714		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2005090473	A1	20050428	US 2004-930743	20040901
PRIORITY APPLN. INFO.:			US 2003-499365P	P 20030903

AB Methods and formulations for treating inflammatory bowel disease are disclosed. The methods and formulations include, but are not limited to, methods and formulations for delivering effective concns. of 4-aminosalicylic acid and/or 5-aminosalicylic acid to affected areas of the **intestine**. The methods and formulations comprise modified-release elements, providing for drug

delivery to the affected or desired area. Diseases and conditions treatable with the present invention include Crohn's disease and **ulcerative colitis**. Thus a matrix tablet contained (mg/tab): 4-aminosalicylate sodium 571.76; lactose 78.12; Avicel PH101 78.12; Methocel Premium CR 200.00; silica 2.00; stearic acid 20.0; PVP 50.0. The pH-dependent coating included (wt./wt.%): Eudragit L100 6.39; Acetyl tri-Bu citrate 1.60; water 3.26; ethanol 88.75.

- IC ICM A61K031-655
- ICS A61K031-606; A61P001-06; C07C245-08; A61K009-20; A61K009-28; A61K009-50
- CC 63-6 (Pharmaceuticals)
- Section cross-reference(s): 1
- ST aminosaliclylate controlled release coated tablet inflammatory **bowel** disease
- IT Inflammation  
(Crohn's disease; controlled-release formulations of aminosaliclylates for treating inflammatory **bowel** disease)
- IT **Intestine**, disease  
(Crohn's; controlled-release formulations of aminosaliclylates for treating inflammatory **bowel** disease)
- IT Polymers, biological studies  
(cellulosic, controlled-release, Methocel Premium CR; controlled-release formulations of aminosaliclylates for treating inflammatory **bowel** disease)
- IT Absorbents
- Buffers
- Coating materials
- Coating process
- Dissolution
- Dyes
- Fillers
- Humectants
- Lubricants
- Pharmacokinetics
- Plasticizers
- Preservatives
- Urine analysis
- Wetting agents
- pH  
(controlled-release formulations of aminosaliclylates for treating inflammatory **bowel** disease)
- IT Drug delivery systems  
(controlled-release, modified-, delayed-, and extended-release; controlled-release formulations of aminosaliclylates for treating inflammatory **bowel** disease)
- IT **Intestine**, disease

- (inflammatory; controlled-release formulations of aminosalicylates for treating inflammatory **bowel** disease)
- IT Acids, biological studies  
(org.; controlled-release formulations of aminosalicylates for treating inflammatory **bowel** disease)
- IT Membranes, nonbiological  
(semipermeable, in drug formulation; controlled-release formulations of aminosalicylates for treating inflammatory **bowel** disease)
- IT Drug delivery systems  
(sustained-release; controlled-release formulations of aminosalicylates for treating inflammatory **bowel** disease)
- IT Drug delivery systems  
(tablet disintegrant; controlled-release formulations of aminosalicylates for treating inflammatory **bowel** disease)
- IT Drug delivery systems  
(tablets, coated; controlled-release formulations of aminosalicylates for treating inflammatory **bowel** disease)
- IT Inflammation  
Intestine, disease  
(ulcerative colitis; controlled-release formulations of aminosalicylates for treating inflammatory **bowel** disease)
- IT 242126-56-3  
(controlled-release formulations of aminosalicylates for treating inflammatory **bowel** disease)
- IT 95710-87-5  
(controlled-release formulations of aminosalicylates for treating inflammatory **bowel** disease)
- IT 7640-38-2  
(controlled-release formulations of aminosalicylates for treating inflammatory **bowel** disease)
- IT 57-11-4, Stearic acid, biological studies 63-42-3, Lactose  
77-90-7, Acetyl tributyl citrate 109-43-3 557-04-0, Magnesium stearate 7631-86-9, Silica, biological studies 9003-39-8, PVP  
9004-34-6, Avicel PH101, biological studies 9004-57-3, Ethocel  
9063-38-1, Sodium starch glycolate 14807-96-6, Talc, biological studies 25086-15-1, Eudragit L100 25086-48-0 33434-24-1, Eudragit RS 12.5  
(controlled-release formulations of aminosalicylates for treating inflammatory **bowel** disease)
- IT 65-49-6, 4-Aminosalicylic acid  
(controlled-release formulations of aminosalicylates for treating inflammatory **bowel** disease)

IT 89-57-6, 5-Aminosalicylic acid 89-57-6D, salts and esters  
15722-48-2, 5,5'-Azo-bis salicylic acid 15722-48-2D, 5,5'-Azo-bis  
salicylic acid, salts of 95710-82-0 95710-82-0D, salts of  
(controlled-release formulations of aminosaliclates for treating  
inflammatory bowel disease)  
IT 7647-01-0, Hydrogen chloride, biological studies  
(testing medium; controlled-release formulations of  
aminosalicylates for treating inflammatory bowel  
disease)

L21 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:780526 HCAPLUS

DOCUMENT NUMBER: 141:289059

TITLE: Treatment of **intestinal** conditions  
with N-2,3,3-tetramethylbicyclo[2.2.1]heptan-2-  
amine

INVENTOR(S): Devane, John

PATENT ASSIGNEE(S): Athpharma Limited, Ire.

SOURCE: PCT Int. Appl., 83 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004080446	A1	20040923	WO 2004-IB1134	200403 12
WO 2004080446	B1	20041209		
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RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2518385	AA	20040923	CA 2004-2518385	200403 12
US 2004209961	A1	20041021	US 2004-798421	

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12

EP 1603544 A1 20051214 EP 2004-720110

200403  
12R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,  
PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU,  
PL, SK

PRIORITY APPLN. INFO.:

US 2003-454527P P

200303  
14

WO 2004-IB1134 W

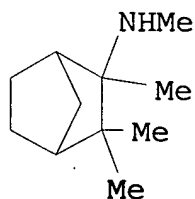
200403  
12

AB The invention discloses methods and formulations for reducing, preventing, and/or managing abnormal increases in **gastrointestinal** motility, and **intestinal** conditions that cause the same. Methods of using N-2,3,3-tetramethylbicyclo-[2.2.1]heptane-2-amine and formulations comprising N-2,3,3-tetramethylbicyclo-[2.2.1]heptan-2-amine are included.

IT 60-40-2  
(tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)

RN 60-40-2 HCAPLUS

CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl- (9CI) (CA INDEX NAME)



IT 107538-05-6 107538-06-7 760175-93-7  
760175-94-8 760175-95-9 760175-96-0  
760175-97-1 760175-98-2 760175-99-3  
760176-00-9 760176-01-0 760176-02-1  
760176-03-2 760176-04-3 760176-05-4  
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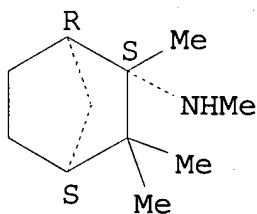
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760176-24-7 760176-25-8 760176-27-0  
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760176-34-9 760176-35-0 760176-36-1  
760176-37-2 760176-38-3 760176-39-4  
760176-40-7 760176-41-8 760176-42-9  
760176-43-0 760176-44-1 760176-45-2

(tetramethylbicycloheptanamine for modulating  
gastrointestinal motility and treating **intestinal**  
conditions, and combinations with other agents)

RN 107538-05-6 HCAPLUS

CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, (1R,2S,4S) -  
(9CI) (CA INDEX NAME)

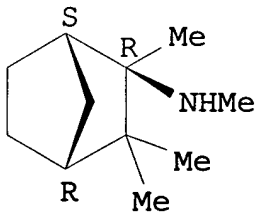
Absolute stereochemistry.



RN 107538-06-7 HCAPLUS

CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, (1S,2R,4R) -  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

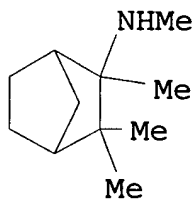


RN 760175-93-7 HCAPLUS

CN 1,6-Hexanediaminium, N,N,N,N',N',N'-hexamethyl-, mixt. with  
N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX  
NAME)

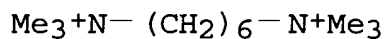
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CMF C11 H21 N



CM 2

CRN 60-26-4  
CMF C12 H30 N2

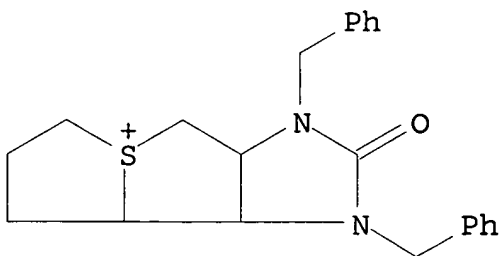


RN 760175-94-8 HCAPLUS  
CN Thieno[1',2':1,2]thieno[3,4-d]imidazol-5-ium, decahydro-2-oxo-1,3-bis(phenylmethyl)-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

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CRN 7187-66-8  
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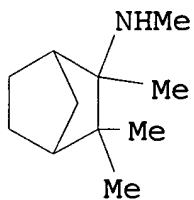
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CMF C11 H21 N



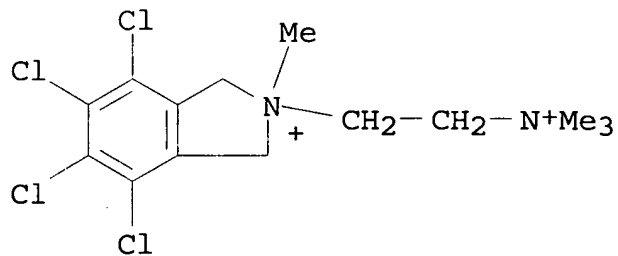
RN 760175-95-9 HCAPLUS

CN 1H-Isoindolium, 4,5,6,7-tetrachloro-2,3-dihydro-2-methyl-2-[2-(trimethylammonio)ethyl]-, dichloride, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

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CRN 69-27-2

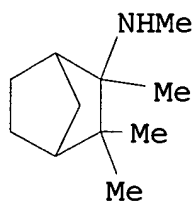
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● 2 Cl<sup>-</sup>

CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760175-96-0 HCAPLUS

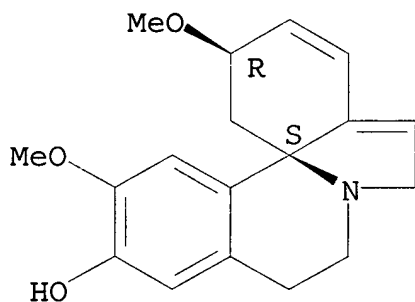
CN Erythrinan-16-ol, 1,2,6,7-tetrahydro-3,15-dimethoxy-, (3.beta.)-,  
mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI)  
(CA INDEX NAME)

CM 1

CRN 7290-03-1

CMF C18 H21 N O3

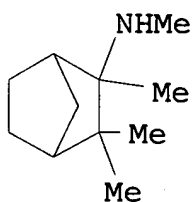
Absolute stereochemistry.



CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760175-97-1 HCAPLUS

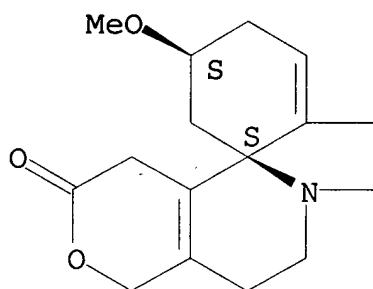
CN 1H,12H-Benzo[i]pyrano[3,4-g]indolizin-12-one, 2,3,5,6,8,9,10,13-octahydro-2-methoxy-, (2S,13bS)-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

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CRN 23255-54-1

CMF C16 H21 N O3

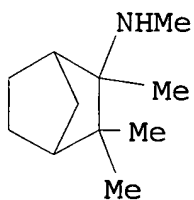
Absolute stereochemistry.



CM 2

CRN 60-40-2

CMF C11 H21 N



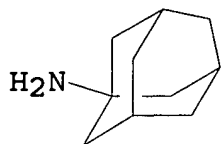
RN 760175-98-2 HCAPLUS

CN Tricyclo[3.3.1.1<sup>3,7</sup>]decan-1-amine, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 768-94-5

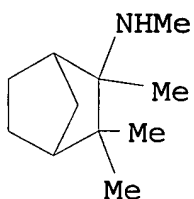
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CM 2

CRN 60-40-2

CMF C11 H21 N



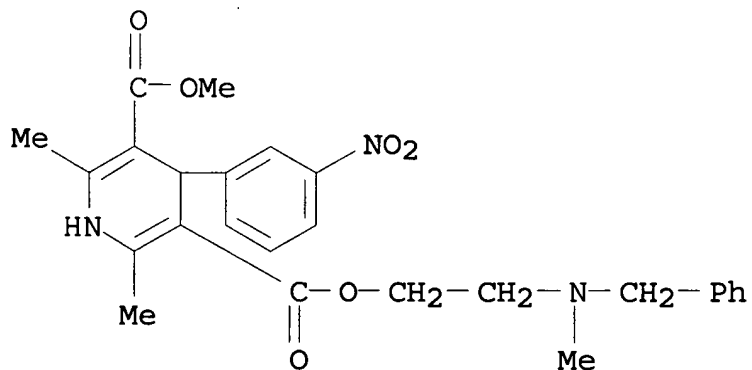
RN 760175-99-3 HCAPLUS

CN 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl 2-[methyl(phenylmethyl)amino]ethyl ester, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 55985-32-5

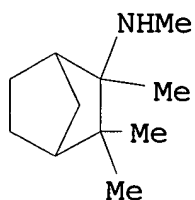
CMF C26 H29 N3 O6



CM 2

CRN 60-40-2

CMF C11 H21 N



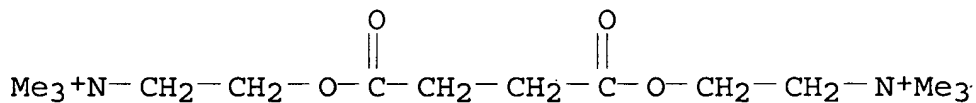
RN 760176-00-9 HCAPLUS

CN Ethanaminium, 2,2'-[(1,4-dioxo-1,4-butanediyl)bis(oxy)]bis[N,N,N-trimethyl-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 306-40-1

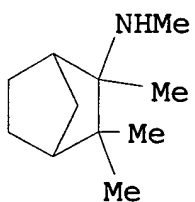
CMF C14 H30 N2 O4



CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760176-01-0 HCAPLUS

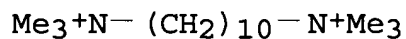
CN 1,10-Decanediaminium, N,N,N,N',N',N'-hexamethyl-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

NAME)

CM 1

CRN 156-74-1

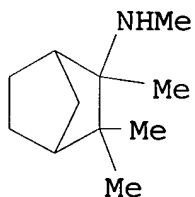
CMF C16 H38 N2



CM 2

CRN 60-40-2

CMF C11 H21 N



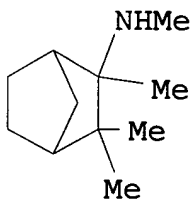
RN 760176-02-1 HCAPLUS

CN 13H-4,6:21,24-Dietheno-8,12-metheno-1H-pyrido[3',2':14,15][1,11]diox  
acycloeicosino[2,3,4-ij]isoquinolinium, 2,3,13a,14,15,16,25,25a-  
octahydro-9,19-dihydroxy-18,29-dimethoxy-1,14,14-trimethyl-,  
(13aR,25aS)-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-  
amine (9CI) (CA INDEX NAME)

CM 1

CRN 60-40-2

CMF C11 H21 N



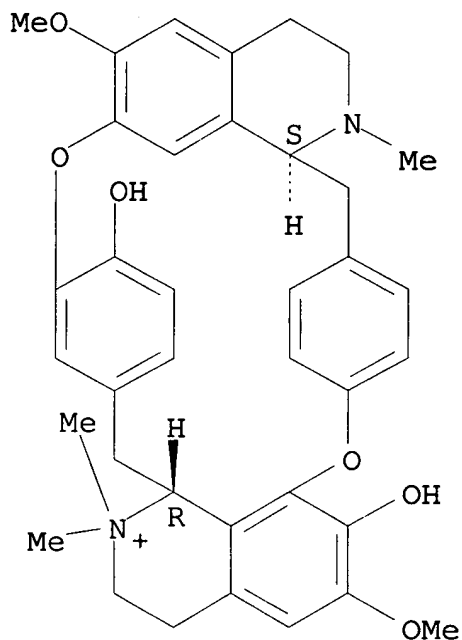


CM 2

CRN 57-95-4

CMF C37 H41 N2 O6

Absolute stereochemistry.



RN .760176-03-2 HCAPLUS

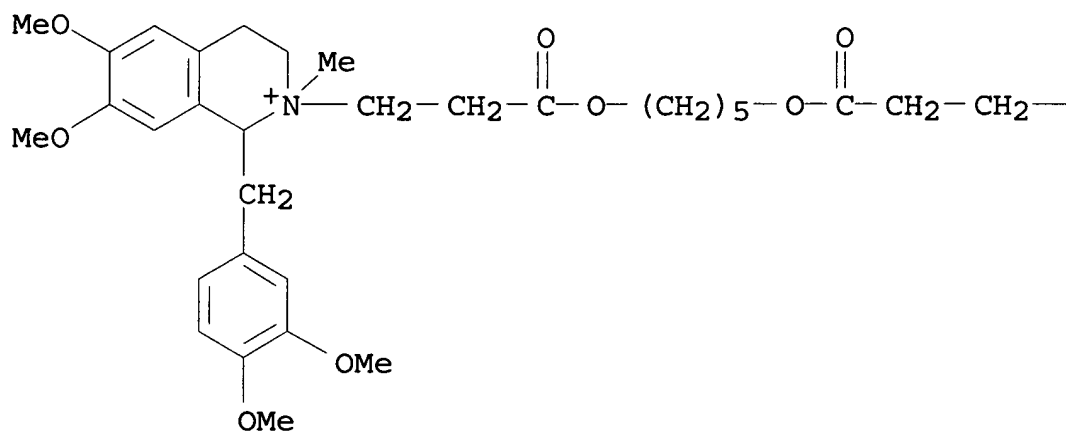
CN Isoquinolinium, 2,2'-[1,5-pentanediyldis[oxy(3-oxo-3,1-propanediyl)]]bis[1-[(3,4-dimethoxyphenyl)methyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

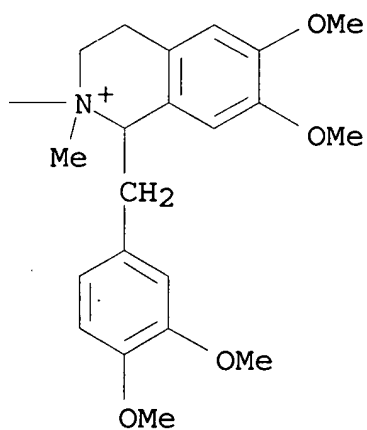
CRN 64228-79-1

CMF C53 H72 N2 O12

PAGE 1-A



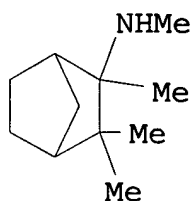
PAGE 1-B



CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760176-04-3 HCAPLUS

CN Isoquinolinium, 2,2'-[(1,4-dioxo-1,4-butanediyl)bis(oxy-3,1-propanediyl)]bis[1,2,3,4-tetrahydro-6,7,8-trimethoxy-2-methyl-1-[(3,4,5-trimethoxyphenyl)methyl]-, (1R,1'R,2S,2'S)-rel-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

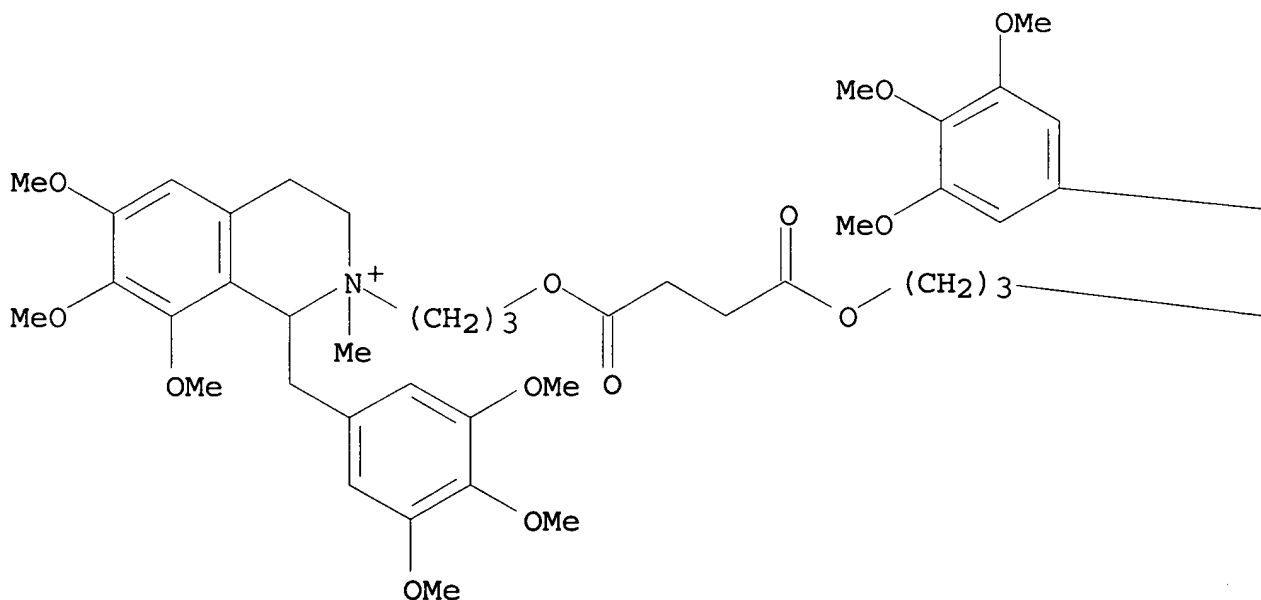
CM 1

CRN 133814-18-3

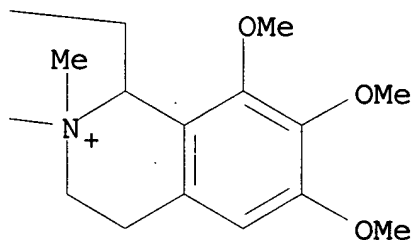
CMF C56 H78 N2 O16

Currently available stereo shown.

PAGE 1-A



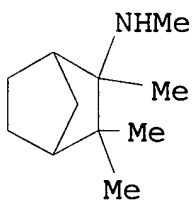
PAGE 1-B



CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760176-05-4 HCAPLUS

CN Isoquinolinium, 2,2'-[[[(4E)-1,8-dioxo-4-octene-1,8-diyl]bis(oxy-3,1-propanediyl)]bis[1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-1-[(3,4,5-trimethoxyphenyl)methyl]-, (1R,1'R)-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

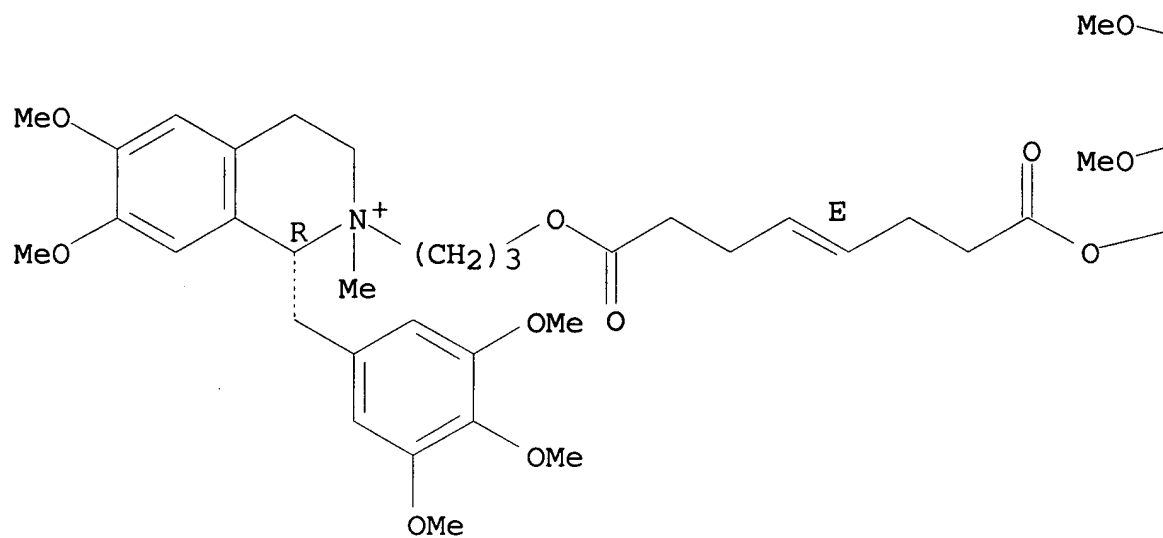
CM 1

CRN 133814-19-4

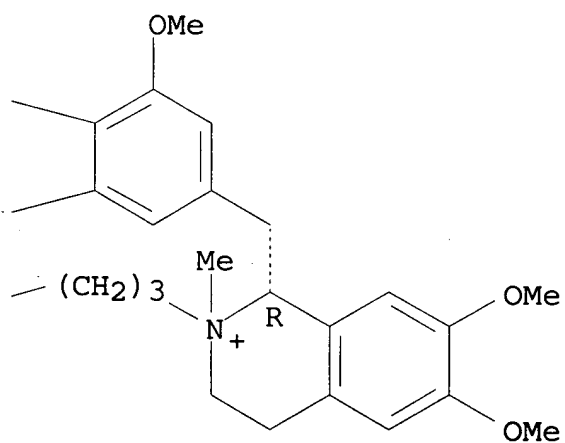
CMF C58 H80 N2 O14

Absolute stereochemistry.  
Double bond geometry as shown.

PAGE 1-A



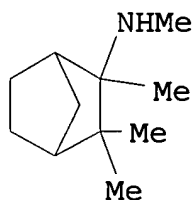
PAGE 1-B



CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760176-06-5 HCAPLUS

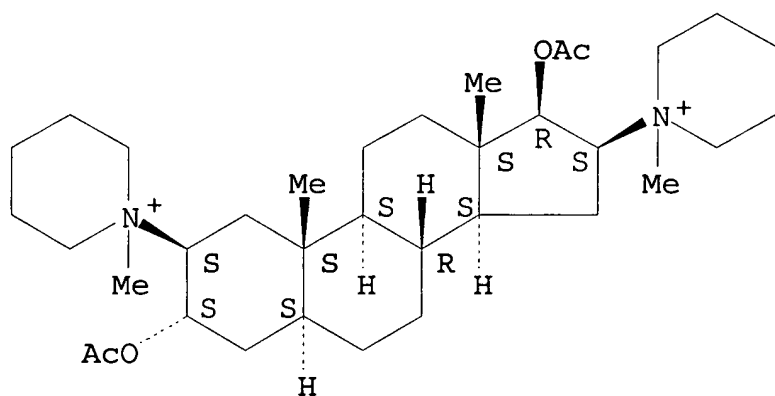
CN Piperidinium, 1,1'-[(2.beta.,3.alpha.,5.alpha.,16.beta.,17.beta.)-3,17-bis(acetyloxy)androstane-2,16-diyl]bis[1-methyl-, dibromide, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 15500-66-0

CMF C35 H60 N2 O4 . 2 Br

Absolute stereochemistry.

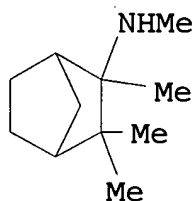


● 2 Br<sup>-</sup>

CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760176-07-6 HCAPLUS

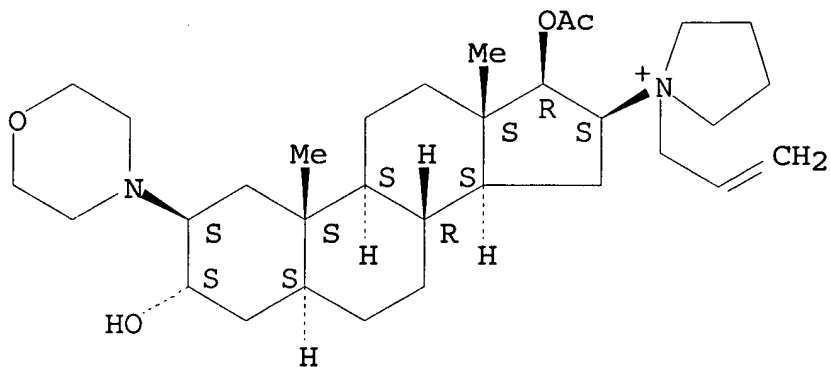
CN Pyrrolidinium, 1-[(2.beta.,3.alpha.,5.alpha.,16.beta.,17.beta.)-17-(acetyloxy)-3-hydroxy-2-(4-morpholinyl)androstan-16-yl]-1-(2-propenyl)-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 143558-00-3

CMF C32 H53 N2 O4

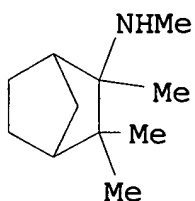
Absolute stereochemistry.



CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760176-08-7 HCAPLUS

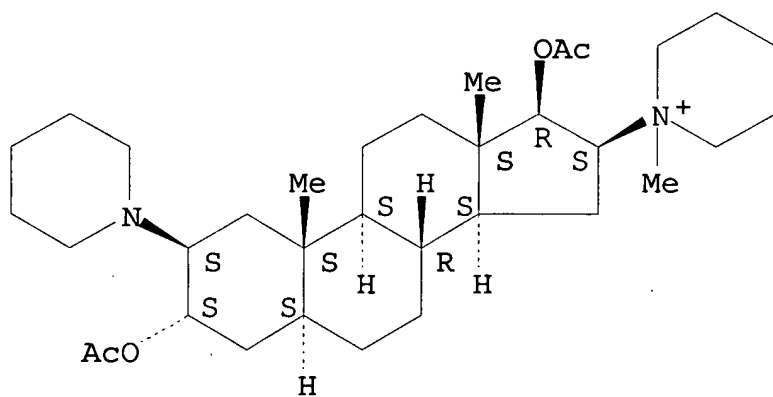
CN Piperidinium, 1-[(2.beta.,3.alpha.,5.alpha.,16.beta.,17.beta.)-3,17-bis(acetyloxy)-2-(1-piperidinylandrostan-16-yl]-1-methyl-, bromide, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI)  
(CA INDEX NAME)

CM 1

CRN 50700-72-6

CMF C34 H57 N2 O4 . Br

Absolute stereochemistry.



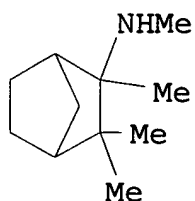
● Br<sup>-</sup>

CM 2

CRN 60-40-2

CMF C11 H21 N





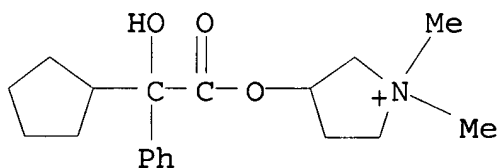
RN 760176-09-8 HCAPLUS

CN Pyrrolidinium, 3-[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethyl-  
; bromide, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-  
amine (9CI) (CA INDEX NAME)

CM 1

CRN 596-51-0

CMF C19 H28 N O3 . Br

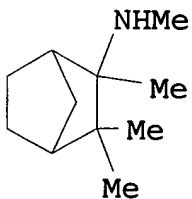


● Br<sup>-</sup>

CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760176-10-1 HCAPLUS

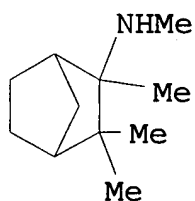
CN Benzeneacetic acid, .alpha.-(hydroxymethyl)- (3-endo)-8-methyl-8-

azabicyclo[3.2.1]oct-3-yl ester, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 60-40-2

CMF C11 H21 N

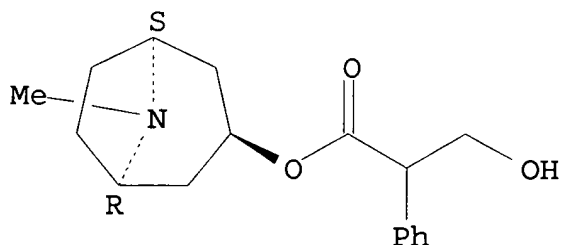


CM 2

CRN 51-55-8

CMF C17 H23 N O3

Relative stereochemistry.



RN 760176-11-2 HCAPLUS

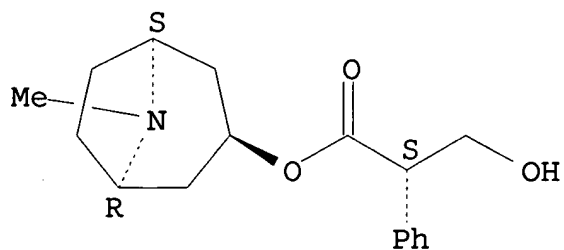
CN Benzeneacetic acid, .alpha.-(hydroxymethyl)-, (3-endo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl ester, (.alpha.S)-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 101-31-5

CMF C17 H23 N O3

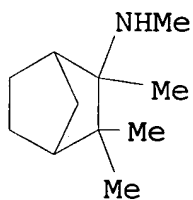
Absolute stereochemistry. Rotation (-).



CM 2

CRN 60-40-2

CMF C11 H21 N



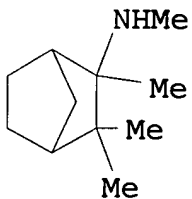
RN 760176-12-3 HCAPLUS

CN Benzeneacetic acid, .alpha.-(hydroxymethyl)-,  
 (1.alpha.,2.beta.,4.beta.,5.alpha.,7.beta.)-9-methyl-3-oxa-9-  
 azatricyclo[3.3.1.0<sup>2,4</sup>]non-7-yl ester, (.alpha.S)-, mixt. with  
 N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX  
 NAME)

CM 1

CRN 60-40-2

CMF C11 H21 N

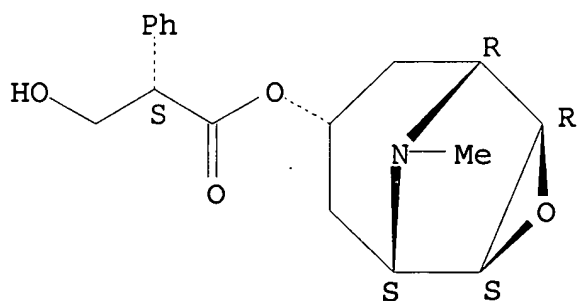


CM 2

CRN 51-34-3

CMF C17 H21 N O4

Absolute stereochemistry. Rotation (-).



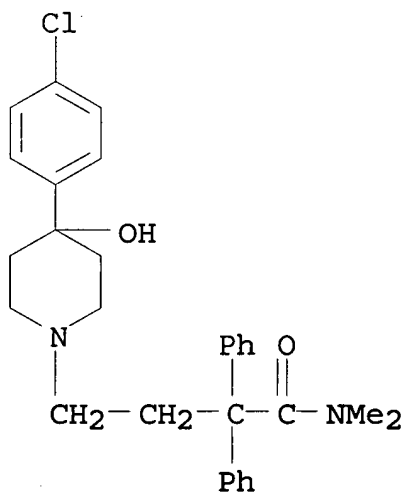
RN 760176-13-4 HCAPLUS

CN 1-Piperidinebutanamide, 4-(4-chlorophenyl)-4-hydroxy-N,N-dimethyl-.alpha.,.alpha.-diphenyl-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 53179-11-6

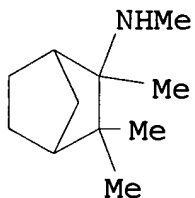
CMF C29 H33 Cl N2 O2



CM 2

CRN 60-40-2

CMF C11 H21 N



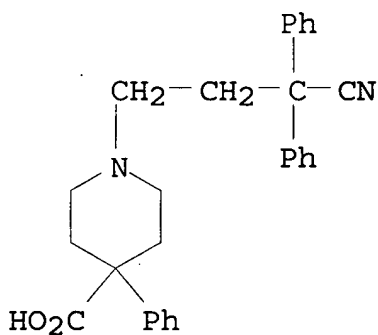
RN 760176-14-5 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-(3-cyano-3,3-diphenylpropyl)-4-phenyl-  
, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI)  
(CA INDEX NAME)

CM 1

CRN 28782-42-5

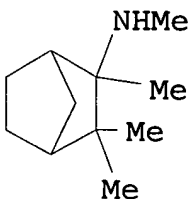
CMF C28 H28 N2 O2



CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760176-15-6 HCAPLUS

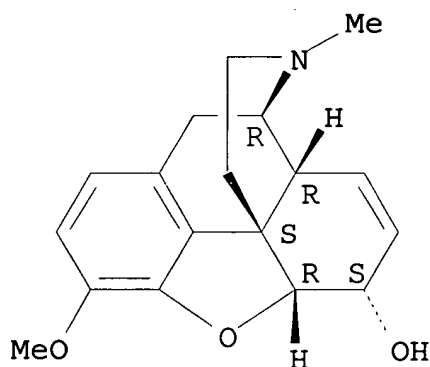
CN Morphinan-6-ol, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-,  
(5.alpha.,6.alpha.)-, mixt. with N,2,3,3-  
tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 76-57-3

CMF C18 H21 N O3

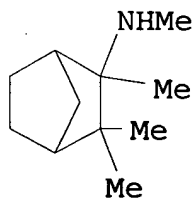
Absolute stereochemistry.



CM 2

CRN 60-40-2

CMF C11 H21 N

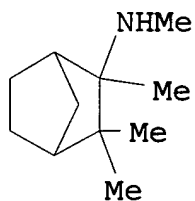


RN 760176-16-7 HCAPLUS

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-  
(5.alpha.,6.alpha.)-, mixt. with N,2,3,3-  
tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

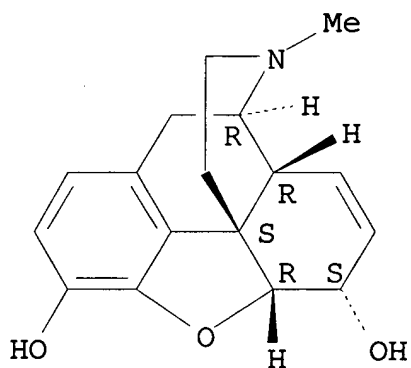
CRN 60-40-2  
CMF C11 H21 N



CM 2

CRN 57-27-2  
CMF C17 H19 N O3

Absolute stereochemistry. Rotation (-).

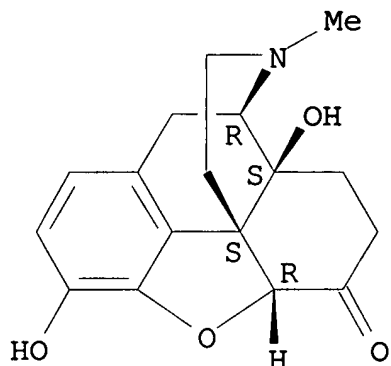


RN 760176-17-8 HCAPLUS  
CN Morphinan-6-one, 4,5-epoxy-3,14-dihydroxy-17-methyl-, (5.alpha.)-,  
mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI)  
(CA INDEX NAME)

CM 1

CRN 76-41-5  
CMF C17 H19 N O4

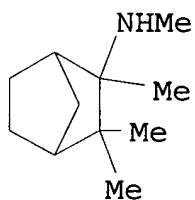
Absolute stereochemistry.



CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760176-18-9 HCAPLUS

CN Morphinan-6-one, 4,5-epoxy-14-hydroxy-3-methoxy-17-methyl-, hydrochloride, (5.alpha.)-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

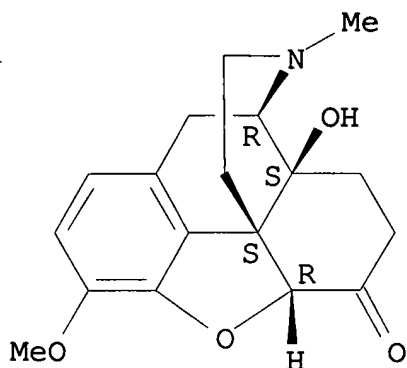
CM 1

CRN 124-90-3

CMF C18 H21 N O4 . Cl H

Absolute stereochemistry.



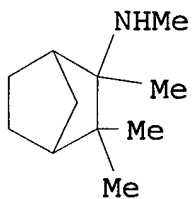


● HCl

CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760176-19-0 HCAPLUS

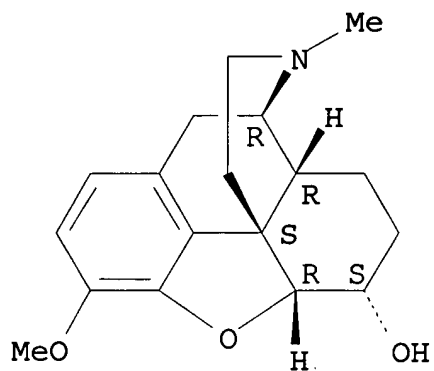
CN Morphinan-6-ol, 4,5-epoxy-3-methoxy-17-methyl-, (5.alpha.,6.alpha.)-  
, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI)  
(CA INDEX NAME)

CM 1

CRN 125-28-0

CMF C18 H23 N O3

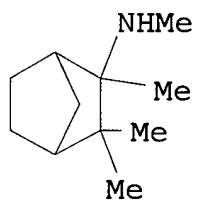
Absolute stereochemistry.



CM 2

CRN 60-40-2

CMF C11 H21 N



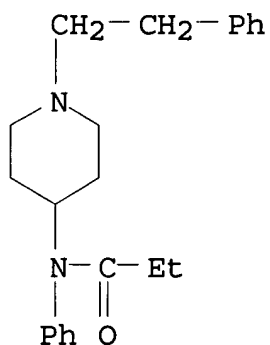
RN 760176-20-3 HCAPLUS

CN Propanamide, N-phenyl-N-[1-(2-phenylethyl)-4-piperidinyl]-, mixt.  
with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA  
INDEX NAME)

CM 1

CRN 437-38-7

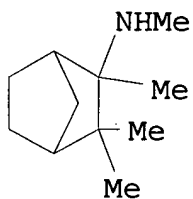
CMF C22 H28 N2 O



CM 2

CRN 60-40-2

CMF C11 H21 N



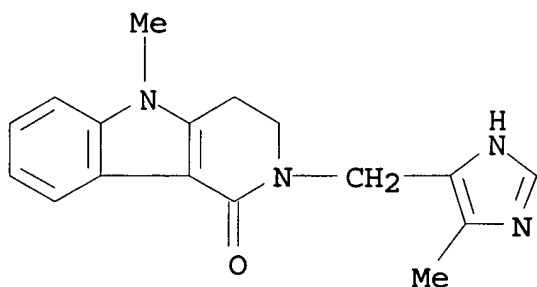
RN 760176-21-4 HCAPLUS

CN 1H-Pyrido[4,3-b]indol-1-one, 2,3,4,5-tetrahydro-5-methyl-2-[(5-methyl-1H-imidazol-4-yl)methyl]-, monohydrochloride, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 122852-69-1

CMF C17 H18 N4 O . Cl H

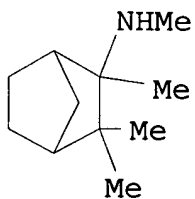


● HCl

CM 2

CRN 60-40-2

CMF C11 H21 N



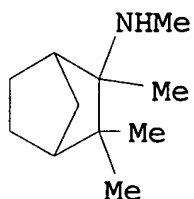
RN 760176-22-5 HCAPLUS

CN Benzeneacetonitrile, .alpha.-[3-[[2-(3,4-dimethoxyphenyl)ethyl]methylamino]propyl]-3,4-dimethoxy-.alpha.-(1-methylethyl)-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 60-40-2

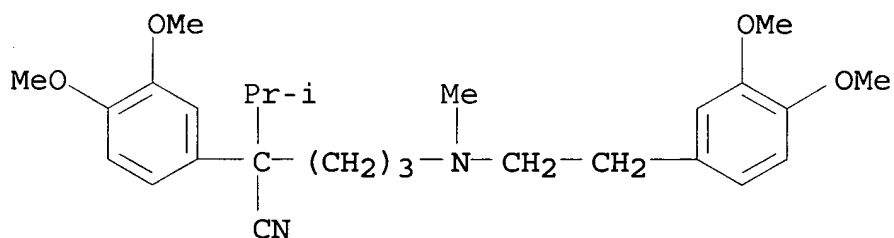
CMF C11 H21 N



CM 2

CRN 52-53-9

CMF C27 H38 N2 O4



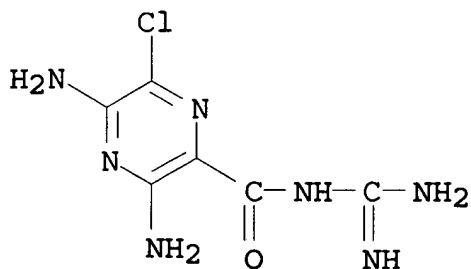
RN 760176-23-6 HCAPLUS

CN Pyrazinecarboxamide, 3,5-diamino-N-(aminoiminomethyl)-6-chloro-,  
 mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI)  
 (CA INDEX NAME)

CM 1

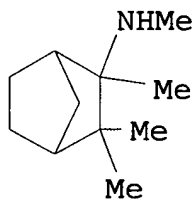
CRN 2609-46-3

CMF C6 H8 Cl N7 O



CM 2

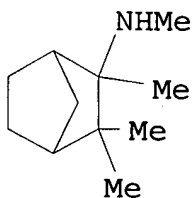
CRN 60-40-2  
CMF C11 H21 N



RN 760176-24-7 HCAPLUS  
CN Benzoic acid, 5-(aminosulfonyl)-4-chloro-2-[(2-furanylmethyl)amino]-  
, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI)  
(CA INDEX NAME)

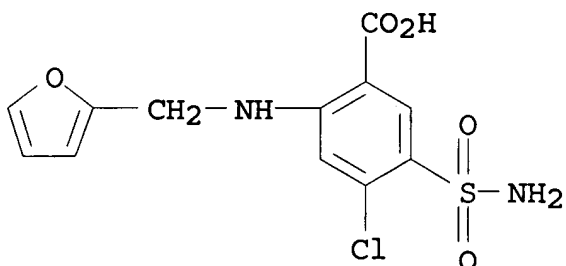
CM 1

CRN 60-40-2  
CMF C11 H21 N



CM 2

CRN 54-31-9  
CMF C12 H11 Cl N2 O5 S



RN 760176-25-8 HCAPLUS  
CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, mixt. with  
bismuth (9CI) (CA INDEX NAME)

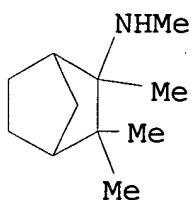
CM 1

CRN 7440-69-9  
CMF Bi

Bi

CM 2

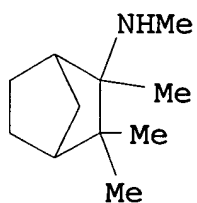
CRN 60-40-2  
CMF C11 H21 N



RN 760176-27-0 HCAPLUS  
CN L-Cysteinamide, D-phenylalanyl-L-cysteiny-L-phenylalanyl-D-  
tryptophyl-L-lysyl-L-threonyl-N-[(1R,2R)-2-hydroxy-1-  
(hydroxymethyl)propyl]-, cyclic (2.fwdarw.7)-disulfide, monoacetate  
(salt), mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine  
(9CI) (CA INDEX NAME)

CM 1

CRN 60-40-2  
CMF C11 H21 N



CM 2

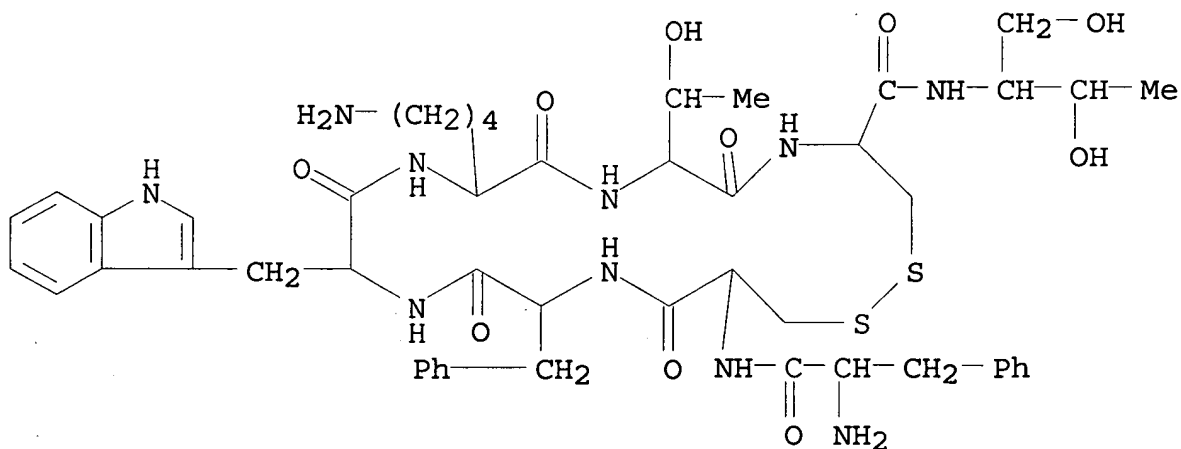
CRN 760176-26-9

CMF C49 H66 N10 O10 S2 . C2 H4 O2

CM 3

CRN 83150-76-9

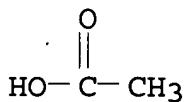
CMF C49 H66 N10 O10 S2



CM 4

CRN 64-19-7

CMF C2 H4 O2





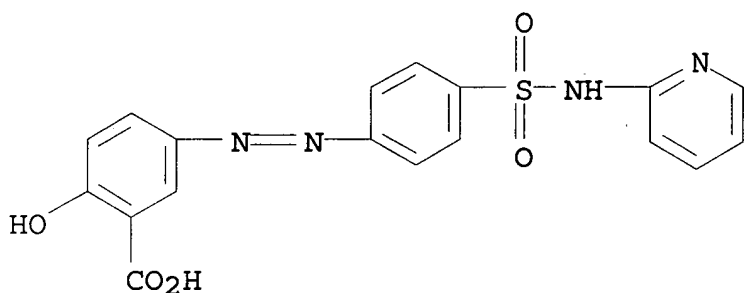
RN 760176-28-1 HCAPLUS

CN Benzoic acid, 2-hydroxy-5-[[4-[(2-pyridinylamino)sulfonyl]phenyl]azo]-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI)  
(CA INDEX NAME)

CM 1

CRN 599-79-1

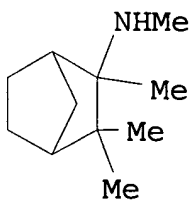
CMF C18 H14 N4 O5 S



CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760176-29-2 HCAPLUS

CN Pregna-1,4-diene-3,11,20-trione, 17,21-dihydroxy-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 60-40-2

CMF C11 H21 N

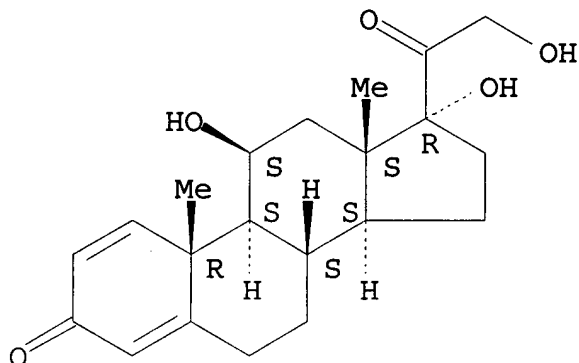


CM 2

CRN 50-24-8

CMF C21 H28 O5

Absolute stereochemistry.



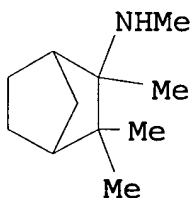
RN 760176-31-6 HCAPLUS

CN Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11.beta.)-, mixt.  
with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA  
INDEX NAME)

CM 1

CRN 60-40-2

CMF C11 H21 N

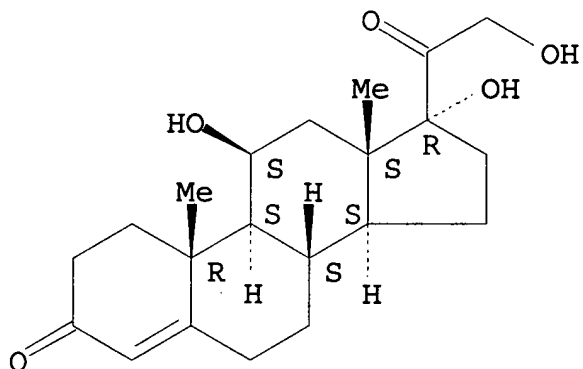


CM 2

CRN 50-23-7

CMF C21 H30 O5

Absolute stereochemistry.



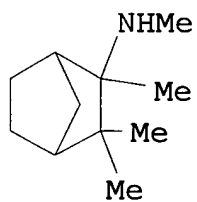
RN 760176-32-7 HCAPLUS

CN Pregn-4-ene-3,11,20-trione, 17,21-dihydroxy-, mixt. with  
N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX  
NAME)

CM 1

CRN 60-40-2

CMF C11 H21 N

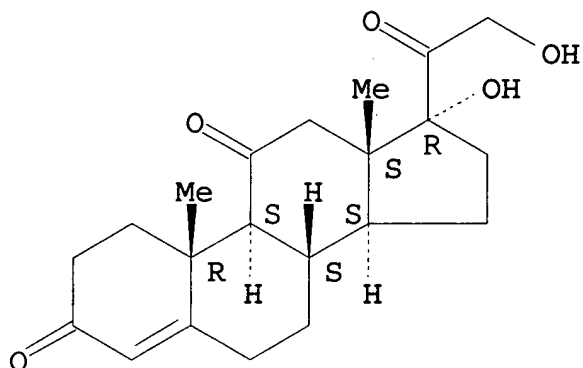


CM 2

CRN 53-06-5

CMF C21 H28 O5

Absolute stereochemistry.



RN 760176-33-8 HCAPLUS

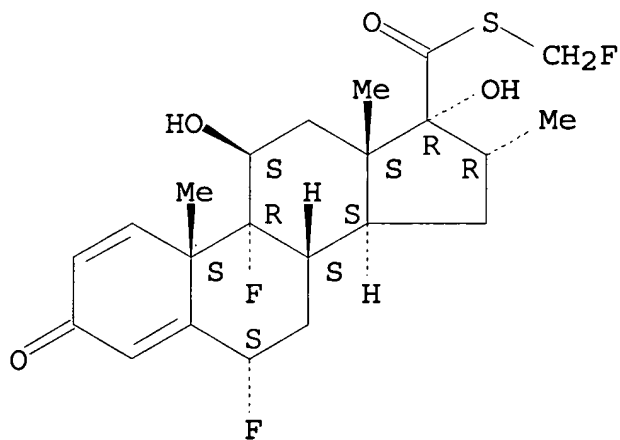
CN Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11,17-dihydroxy-16-methyl-3-oxo-, S-(fluoromethyl) ester, (6.alpha.,11.beta.,16.alpha.,17.alpha.)-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 90566-53-3

CMF C22 H27 F3 O4 S

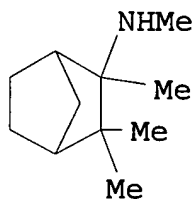
Absolute stereochemistry.



CM 2

CRN 60-40-2

CMF C11 H21 N



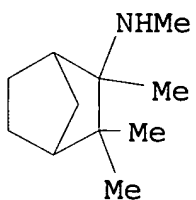
RN 760176-34-9 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11.beta.,16.alpha.)-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 60-40-2

CMF C11 H21 N

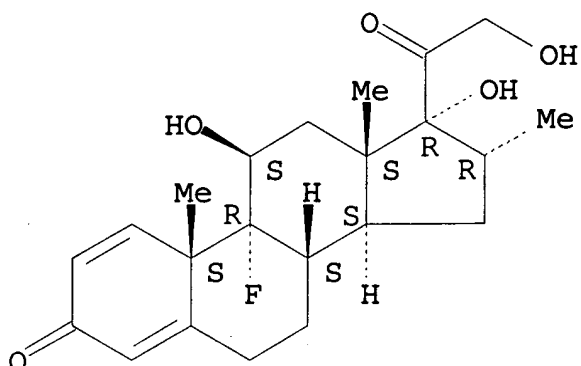


CM 2

CRN 50-02-2

CMF C22 H29 F O5

Absolute stereochemistry.



RN 760176-35-0 HCAPLUS

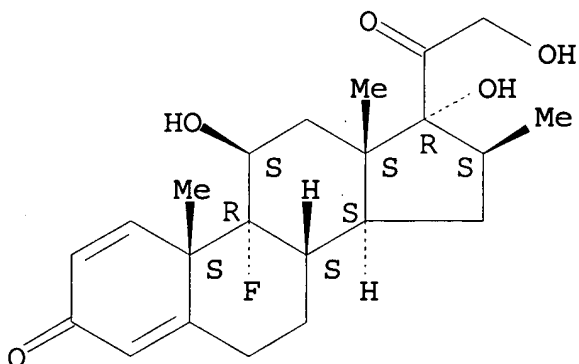
CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11.beta.,16.beta.)-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 378-44-9

CMF C22 H29 F O5

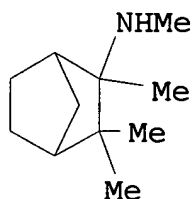
Absolute stereochemistry.



CM 2

CRN 60-40-2

CMF C11 H21 N



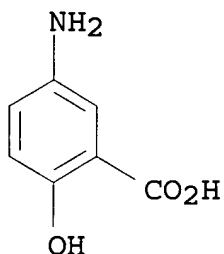
RN 760176-36-1 HCAPLUS

CN Benzoic acid, 5-amino-2-hydroxy-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 89-57-6

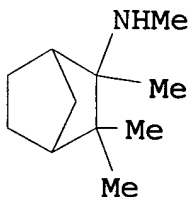
CMF C7 H7 N O3



CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760176-37-2 HCAPLUS

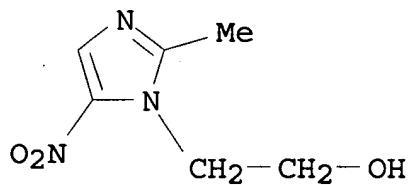
CN 1H-Imidazole-1-ethanol, 2-methyl-5-nitro-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)



CM 1

CRN 443-48-1

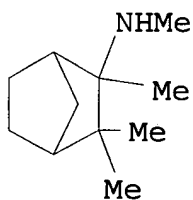
CMF C6 H9 N3 O3



CM 2

CRN 60-40-2

CMF C11 H21 N



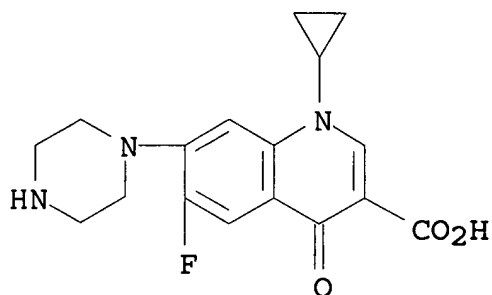
RN 760176-38-3 HCAPLUS

CN 3-Quinolinecarboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 85721-33-1

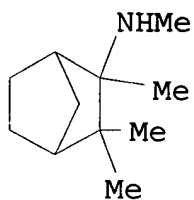
CMF C17 H18 F N3 O3



CM 2

CRN 60-40-2

CMF C11 H21 N



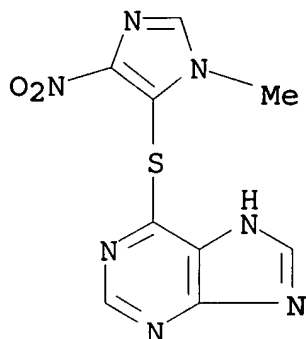
RN 760176-39-4 HCAPLUS

CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, mixt. with  
6-[(1-methyl-4-nitro-1H-imidazol-5-yl)thio]-1H-purine (9CI) (CA  
INDEX NAME)

CM 1

CRN 446-86-6

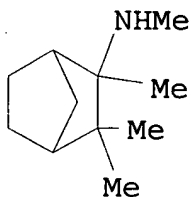
CMF C9 H7 N7 O2 S



CM 2

CRN 60-40-2

CMF C11 H21 N



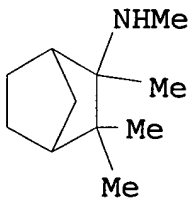
RN 760176-40-7 HCAPLUS

CN 6H-Purine-6-thione, 1,7-dihydro-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

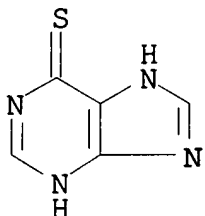
CRN 60-40-2

CMF C11 H21 N



CM 2

CRN 50-44-2  
CMF C5 H4 N4 S



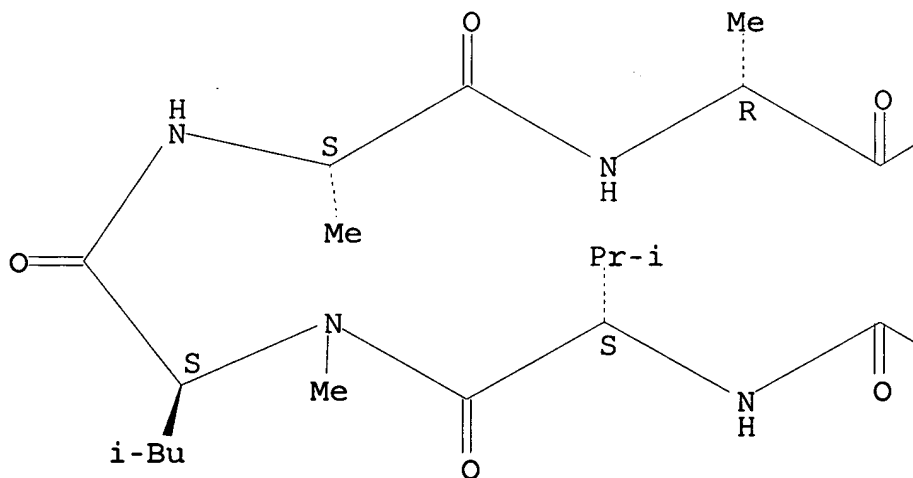
RN 760176-41-8 HCAPLUS  
CN Cyclosporin A, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

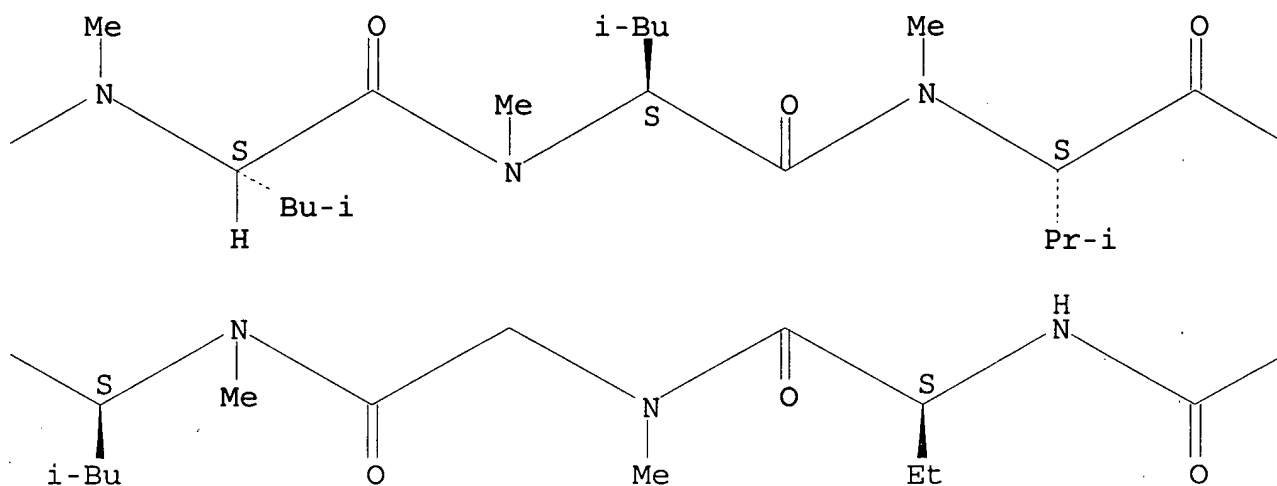
CRN 59865-13-3  
CMF C62 H111 N11 O12

Absolute stereochemistry.  
Double bond geometry as shown.

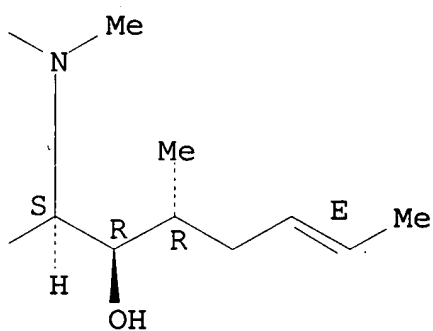
PAGE 1-A



PAGE 1-B



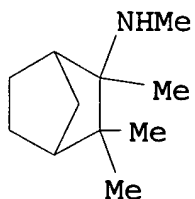
PAGE 1-C



CM 2

CRN 60-40-2

CMF C11 H21 N



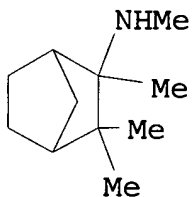
RN 760176-42-9 HCAPLUS

CN L-Glutamic acid, N-[4-[[ (2,4-diamino-6-pteridiny)l)methyl]methylamino]benzoyl]-, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 60-40-2

CMF C11 H21 N

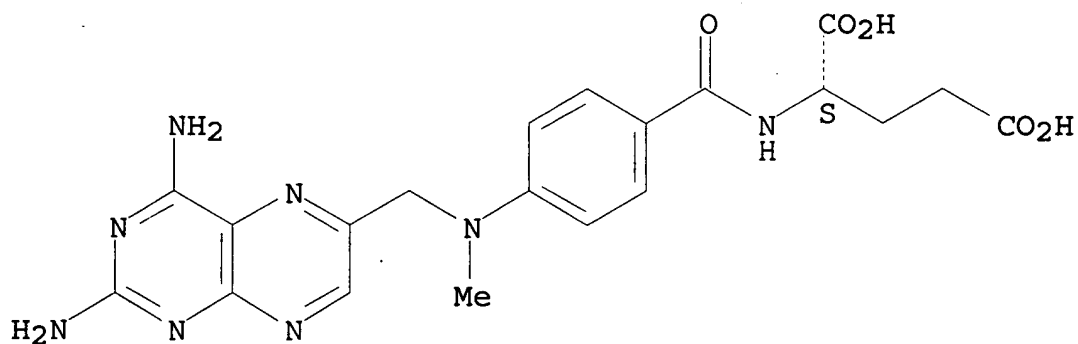


CM 2

CRN 59-05-2

CMF C20 H22 N8 O5

Absolute stereochemistry.



RN 760176-43-0 HCAPLUS

CN Immunoglobulin G, anti-(human tumor necrosis factor), disulfide with human-mouse monoclonal cA2 light chain, dimer, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 170277-31-3

CMF Unspecified

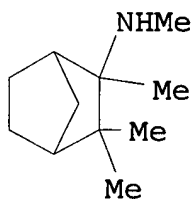
CCI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 60-40-2

CMF C11 H21 N



RN 760176-44-1 HCAPLUS

CN Heparin, mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine (9CI) (CA INDEX NAME)

CM 1

CRN 9005-49-6

CMF Unspecified

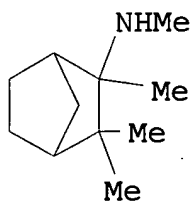
CCI PMS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 60-40-2

CMF C11 H21 N



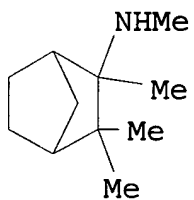
RN 760176-45-2 HCAPLUS

CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, mixt. with  
3-[(2S)-1-methyl-2-pyrrolidinyl]pyridine (9CI) (CA INDEX NAME)

CM 1

CRN 60-40-2

CMF C11 H21 N

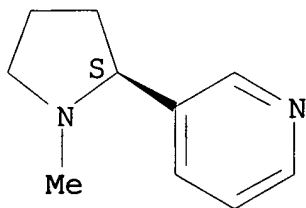


CM 2

CRN 54-11-5

CMF C10 H14 N2

Absolute stereochemistry. Rotation (-).



IC ICM A61K031-135

ICS A61P001-12

CC 1-9 (Pharmacology)

Section cross-reference(s): 63

ST tetramethylbicycloheptanamine **gastrointestinal** motility



- intestinal condition**
- IT Inflammation  
(Crohn's disease, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Intestine, disease**  
(Crohn's, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT Antihistamines  
(H2; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Gastrointestinal motility**  
(agents altering; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT Drug delivery systems  
(buccal; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT Inflammation  
**Intestine, disease**  
(colitis, **spastic, gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Intestine, disease**  
(colon, neurogenic colon, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT Drug delivery systems  
(delayed release; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT Biological transport  
(digestive tract fluid transport, agents altering; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Gastrointestinal motility**  
(disorder, dysmotility; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating

- intestinal** conditions, and combinations with other agents)
- IT Inflammation  
  **Intestine**, disease  
    (**diverticulitis**, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT Inflammation  
  **Intestine**, disease  
    (**enterocolitis**, acute, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT Drug delivery systems  
  (extended-release; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT Fats and Glyceridic oils, biological studies  
  (fish; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT Digestive tract  
  (fluid transport, agents altering; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT Bladder  
  (function; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Intestine**, disease  
  (functional **bowel** disorder, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT Nervous system agents  
  (ganglionic blocking agents; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT Drug delivery systems  
  (immediate-release; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Intestine**, disease

- (inflammatory, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Intestine, disease**  
(irritable **bowel** syndrome, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Intestine**  
(large, infection, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Dysentery**  
(mild, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Drug delivery systems**  
(modified-release; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Drug delivery systems**  
(multiparticulate; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Drug delivery systems**  
(nasal; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Intestine, disease**  
(neurogenic, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Drug delivery systems**  
(oral; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Transport proteins**  
(proton pump, inhibitors; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)
- IT **Stomach**  
(pylorus, **pyloric** spasm, **gastrointestinal**

motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)

IT **Intestine, disease**

(small, infection, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)

IT **Muscle, disease**

(spasm, **abdominal**, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)

IT **Muscle relaxants**

(spasmolytics; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)

IT **Digestive tract, disease**

(**splenic flexure syndrome**, **gastrointestinal** motility increase from; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)

IT **Drug delivery systems**

(sublingual; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)

IT **Drug delivery systems**

(tablets, modified-release; tetramethylbicycloheptanamine for modulating **gastrointestinal** motility and treating **intestinal** conditions, and combinations with other agents)

IT **5-HT agonists**

**5-HT antagonists**

**Antacids**

**Anti-infective agents**

**Anti-inflammatory agents**

**Antidiarrheals**

**Blood pressure**

**Calcium channel blockers**

**Combination chemotherapy**

**Diarrhea**

**Diuretics**

**Drug delivery systems**

**Drug toxicity**

**Gastrointestinal agents**

**Heart rate**

Human  
 Immunomodulators  
 Muscarinic antagonists  
 Nicotinic antagonists  
 Vision  
   (tetramethylbicycloheptanamine for modulating  
   **gastrointestinal** motility and treating **intestinal**  
   conditions, and combinations with other agents)

IT Corticosteroids, biological studies  
 Estrogens  
 Mineralocorticoids  
 Opioids  
 Steroids, biological studies  
   (tetramethylbicycloheptanamine for modulating  
   **gastrointestinal** motility and treating **intestinal**  
   conditions, and combinations with other agents)

IT Drug delivery systems  
   (transdermal; tetramethylbicycloheptanamine for modulating  
   **gastrointestinal** motility and treating **intestinal**  
   conditions, and combinations with other agents)

IT Inflammation  
   **Intestine, disease**  
   (**ulcerative colitis, gastrointestinal**  
   motility increase from; tetramethylbicycloheptanamine for  
   modulating **gastrointestinal** motility and treating  
   **intestinal** conditions, and combinations with other  
   agents)

IT Adrenoceptor antagonists  
   (.beta.-; tetramethylbicycloheptanamine for modulating  
   **gastrointestinal** motility and treating **intestinal**  
   conditions, and combinations with other agents)

IT 60-40-2  
   (tetramethylbicycloheptanamine for modulating  
   **gastrointestinal** motility and treating **intestinal**  
   conditions, and combinations with other agents)

IT 50-02-2, Dexamethasone 50-23-7, Cortisol 50-24-8, Prednisolone  
 50-44-2, 6-Mercaptopurine 51-34-3, Scopolamine 51-55-8,  
 Atropine, biological studies 52-53-9, Verapamil 53-03-2,  
 Prednisone 53-06-5, Cortisone 54-11-5, Nicotine 54-31-9,  
 Furosemide 57-27-2, Morphine, biological studies 57-94-3,  
 Tubocurarine 59-05-2, Methotrexate 60-26-4, Hexamethonium  
 69-27-2 76-41-5, Oxymorphone 76-57-3, Codeine 89-57-6,  
 5-Aminosalicylic acid 101-31-5, Hyoscyamine 124-90-3, Oxycontin  
 125-28-0, Dihydrocodeine 156-74-1, Decamethonium 306-40-1,  
 Succinylcholine 378-44-9, Betamethasone 437-38-7, Fentanyl  
 443-48-1, Metronidazole 446-86-6, Azathioprine 596-51-0,  
 Glycopyrrolate 599-79-1, Sulfasalazine 768-94-5, Amantadine  
 2609-46-3, Amiloride 7187-66-8, Trimethaphan 7290-03-1,

Erysodine 7440-69-9, Bismuth, biological studies 9005-49-6,  
Heparin, biological studies 15500-66-0, Pancuronium 23255-54-1  
28782-42-5, Difenoxine 50700-72-6, Vecuronium 53179-11-6,  
Loperamide 55985-32-5, Peripidine 59865-13-3, Cyclosporine  
64228-79-1, Atracurium 79517-01-4, Sandostatin 85721-33-1,  
Ciprofloxacin 90566-53-3, Fluticasone 107538-05-6  
107538-06-7 122852-69-1, Alosetron hydrochloride  
133814-18-3, Doxacurium 133814-19-4, Mivacurium 143558-00-3,  
Rocuronium 170277-31-3, Remicade 760175-93-7  
760175-94-8 760175-95-9 760175-96-0  
760175-97-1 760175-98-2 760175-99-3  
760176-00-9 760176-01-0 760176-02-1  
760176-03-2 760176-04-3 760176-05-4  
760176-06-5 760176-07-6 760176-08-7  
760176-09-8 760176-10-1 760176-11-2  
760176-12-3 760176-13-4 760176-14-5  
760176-15-6 760176-16-7 760176-17-8  
760176-18-9 760176-19-0 760176-20-3  
760176-21-4 760176-22-5 760176-23-6  
760176-24-7 760176-25-8 760176-27-0  
760176-28-1 760176-29-2 760176-30-5  
760176-31-6 760176-32-7 760176-33-8  
760176-34-9 760176-35-0 760176-36-1  
760176-37-2 760176-38-3 760176-39-4  
760176-40-7 760176-41-8 760176-42-9  
760176-43-0 760176-44-1 760176-45-2

(tetramethylbicycloheptanamine for modulating  
**gastrointestinal** motility and treating **intestinal**  
conditions, and combinations with other agents)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN  
THE RE FORMAT

L21 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:269870 HCAPLUS

DOCUMENT NUMBER: 140:247075

TITLE: Treatment of abnormal increases in  
**gastrointestinal** motility with  
(R)-verapamil

INVENTOR(S): Kelly, John; Devane, John

PATENT ASSIGNEE(S): AGI Therapeutics, Ltd., Ire.

SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of  
U.S. Pat. Appl. 2003 92,765.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO. -----	KIND ----	DATE -----	APPLICATION NO. -----	DATE
US 2004063784	A1	20040401	US 2002-294692	200211 15
US 6849661	B2	20050201		
US 2003092765	A1	20030515	US 2002-256261	200209 27
PRIORITY APPLN. INFO.:			US 2002-256261	B2 200209 27
			US 2001-335959P	P 200111 15

AB The invention discloses methods for treating, preventing, and/or managing abnormal increases in **gastrointestinal** motility, and **intestinal** conditions that cause the same. Such conditions include, but are not limited to, irritable **bowel** syndrome, infectious diseases of the small and large **intestines**, and symptoms of any of the foregoing. In particular, the invention discloses methods of using enriched (R)-verapamil, as well as compns. and formulations contg. the same.

IC ICM A61K031-275

INCL 514526000

CC 1-9 (Pharmacology)

Section cross-reference(s): 63

ST verapamil isomer **gastrointestinal** motility; irritable **bowel** syndrome **gastrointestinal** motility verapamil isomer; infection **intestine gastrointestinal** motility verapamil isomer

IT Artery

(aorta; treatment of abnormal increases in **gastrointestinal** motility with (R)-verapamil)

IT Drug delivery systems

(beads; treatment of abnormal increases in **gastrointestinal** motility with (R)-verapamil)

IT Drug delivery systems

(buccal; treatment of abnormal increases in **gastrointestinal** motility with (R)-verapamil)

IT Drug delivery systems

(caplets; treatment of abnormal increases in **gastrointestinal** motility with (R)-verapamil)

IT Drug delivery systems

- (capsules; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT **Intestine**  
(colon; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(controlled-release; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(granules; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT **Intestine, disease**  
(infection; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Infection  
(intestinal; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT **Intestine, disease**  
(irritable **bowel** syndrome; treatment of abnormal  
increases in **gastrointestinal** motility with  
(R)-verapamil)
- IT Drug delivery systems  
(matrix system; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(membrane-controlled; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(modified-release; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(nasal; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(oral; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(osmotic pumps; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(parenterals; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(particles; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(rectal; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)



- IT Drug delivery systems  
(sachets; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(solids; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(sublingual; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(suppositories; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(suspensions; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(tablets; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
(topical; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Drug delivery systems  
**Gastrointestinal** agents  
**Gastrointestinal** motility  
Vas deferens  
(treatment of abnormal increases in **gastrointestinal**  
motility with (R)-verapamil)
- IT Carbohydrates, biological studies  
Polyesters, biological studies  
Polyoxyalkylenes, biological studies  
Polyurethanes, biological studies  
(treatment of abnormal increases in **gastrointestinal**  
motility with (R)-verapamil)
- IT Drug delivery systems  
(vaginal; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT Polymers, biological studies  
(water-sol. and water-insol.; treatment of abnormal increases in  
**gastrointestinal** motility with (R)-verapamil)
- IT 21829-25-4, Nifedipine 36622-29-4, (S)-Verapamil  
(treatment of abnormal increases in **gastrointestinal**  
motility with (R)-verapamil)
- IT 38321-02-7  
(treatment of abnormal increases in **gastrointestinal**  
motility with (R)-verapamil)
- IT 9002-86-2, Poly (vinyl chloride 9002-88-4, Poly (ethylene  
9002-89-5, Polyvinyl alcohol 9003-20-7, Poly (vinyl acetate  
9003-21-8, Poly (methyl acrylate 9003-39-8, Polyvinylpyrrolidone

9003-42-3, Poly (ethyl methacrylate) 9003-44-5, Poly (vinyl isobutyl ether 9003-63-8, Poly (butyl methacrylate) 9004-34-6, Cellulose, biological studies 9004-35-7, Cellulose acetate 9004-36-8, Cellulose acetate butyrate 9004-38-0, Cellulose acetate phthalate 9004-39-1, Cellulose acetate propionate 9004-48-2, Cellulose propionate 9004-57-3, Ethylcellulose 9004-64-2, Hydroxypropylcellulose 9004-65-3, Hydroxypropylmethylcellulose 9004-67-5, Methylcellulose 9005-25-8, Starch, biological studies 9011-14-7, Poly (methyl methacrylate) 9011-15-8, Poly (isobutyl methacrylate) 9012-09-3, Cellulose triacetate 25038-59-9, Poly (ethylene terephthalate, biological studies 25087-17-6, Poly (hexyl methacrylate) 25189-01-9, Poly (phenyl methacrylate 25322-68-3, Polyethylene glycol 25719-52-2, Poly (lauryl methacrylate) 25986-77-0, Poly (octadecyl acrylate 26124-32-3, Poly (isopropyl acrylate) 26335-74-0, Poly (isobutyl acrylate 33434-24-1, Eudragit RS 30D 37200-12-7, Poly (isodecyl methacrylate 79484-92-7, Methocel

(treatment of abnormal increases in gastrointestinal motility with (R)-verapamil)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2004:220142 HCAPLUS  
DOCUMENT NUMBER: 140:259107  
TITLE: Pharmaceuticals formulations for modified release of statin drugs  
INVENTOR(S): Butler, Jackie; Devane, John; Stark, Paul  
PATENT ASSIGNEE(S): Biovail Laboratories, Inc., Barbados  
SOURCE: PCT Int. Appl., 66 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	
WO 2004021972	A2	20040318	WO 2003-IB4361	20030903
WO 2004021972	A3	20040812		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,			

LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,  
 NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ,  
 TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,  
 BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,  
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
 NE, SN, TD, TG

CA 2497832	AA	20040318	CA 2003-2497832	200309 03
US 2004132802	A1	20040708	US 2003-653469	200309 03
EP 1545503	A2	20050629	EP 2003-794018	200309 03
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006503023	T2	20060126	JP 2004-533786	200309 03
NO 2005000840	A	20050523	NO 2005-840	200502 16
PRIORITY APPLN. INFO.:			US 2002-407270P	P 200209 03
			WO 2003-IB4361	W 200309 03

AB The present invention is directed to compns. and methods of their use in treating, preventing, and/or managing one or more cardiovascular diseases using at least one poorly water-sol. statin, such as, for example, simvastatin and/or lovastatin. One method of the invention involves delaying release of the poorly water-sol. statin for a time sufficient to avoid metab. of the statin at or near the **gastrointestinal** tract wall by the cytochrome P 450 3A metabolic system, and releasing said statin in the ileum, **colon**, or both, with subsequent uptake into the hepatic portal vein and distribution to hepatocytes, wherein HMG-CoA reductase activity may be inhibited with minimal adverse drug interactions. An extended release matrix of simvastatin was prepd. contg Methocel K100LV as the controlled release polymer.

IC ICM A61K

CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1

L21 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2003:551361 HCAPLUS  
DOCUMENT NUMBER: 139:106482  
TITLE: Pravastatin pharmaceutical formulations  
INVENTOR(S): Butler, Jackie; Devane, John; Stark, Paul  
PATENT ASSIGNEE(S): Athpharma Limited, Ire.  
SOURCE: PCT Int. Appl., 83 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057195	A1	20030717	WO 2003-IB336	20030110
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2473106	AA	20030717	CA 2003-2473106	20030110
AU 2003201735	A1	20030724	AU 2003-201735	20030110
US 2003176502	A1	20030918	US 2003-339487	20030110
US 6967218	B2	20051122		
EP 1465605	A1	20041013	EP 2003-700436	20030110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,				

PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU,  
SK

JP 2005519052 T2 20050630 JP 2003-557553 200301  
10

CA 2497896 AA 20040318 CA 2003-2497896 200309  
03

WO 2004021973 A2 20040318 WO 2003-IB4523 200309  
03

WO 2004021973 A3 20040521

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,  
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,  
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,  
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,  
NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,  
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,  
ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,  
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,  
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
NE, SN, TD, TG

US 2004132806 A1 20040708 US 2003-653415 200309  
03

EP 1551356 A2 20050713 EP 2003-748451 200309  
03

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,  
PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU,  
SK

JP 2006504686 T2 20060209 JP 2004-533791 200309  
03

NO 2004003333 A 20040913 NO 2004-3333 200408  
10

NO 2005000933 A 20050418 NO 2005-933 200502  
21

US 2005277691 A1 20051215 US 2005-205028 200508  
17

PRIORITY APPLN. INFO.: US 2002-347775P P 200201  
11

US 2002-407269P	P	200209 03
US 2003-339487	A1	200301 10
WO 2003-IB336	W	200301 10
WO 2003-IB4523	W	200309 03

AB The present invention relates to formulations comprising a therapeutically effective amt. of pravastatin, or a salt. The present formulations and methods are designed to release little or no pravastatin in the stomach but release a therapeutic amt. of pravastatin in the small **intestine**, thereby limiting systemic exposure of the body to pravastatin and maximizing hepatic-specific absorption of the drug. The formulations and methods are particularly useful for treating and/or preventing conditions that are benefited by decreasing levels of lipids and/or cholesterol in the body. Tablets contained pravastatin sodium 5.56, anhyd. lactose 58.74, Avisel PH200 15.0, Methocel E4M 20.0, colloidal SiO<sub>2</sub> 0.20, and Mg stearate 0.50%.

IC ICM A61K009-20

ICS A61K009-22; A61K031-22; A61P003-10; A61P009-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

IT **Intestine**

(small; pravastatin pharmaceutical formulations)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:376402 HCAPLUS

DOCUMENT NUMBER: 138:348722

TITLE: Treatment of abnormal increases in **gastrointestinal** motility with (R)-verapamil

INVENTOR(S): Kelly, John; Devane, John

PATENT ASSIGNEE(S): Ire.

SOURCE: U.S. Pat. Appl. Publ., 19 pp.

DOCUMENT TYPE: CODEN: USXXCO  
 LANGUAGE: Patent  
 FAMILY ACC. NUM. COUNT: English  
 2  
 PATENT INFORMATION:

PATENT NO. -----	KIND ----	DATE -----	APPLICATION NO. -----	DATE
US 2003092765	A1	20030515	US 2002-256261	200209 27
US 2004063784	A1	20040401	US 2002-294692	200211 15
US 6849661	B2	20050201		
CA 2499290	AA	20040422	CA 2002-2499290	200211 15
WO 2004032919	A1	20040422	WO 2002-IB5140	200211 15
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002351118	A1	20040504	AU 2002-351118	200211 15
EP 1542673	A1	20050622	EP 2002-785831	200211 15
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2006504724	T2	20060209	JP 2004-542687	200211 15
NO 2005002026	A	20050426	NO 2005-2026	200504 26

## PRIORITY APPLN. INFO.:

US 2001-335959P

P

200111  
15

US 2002-256261

B2

200209  
27

WO 2002-IB5140

W

200211  
15

AB The present invention is directed to methods of treating, preventing, and/or managing abnormal increases in **gastrointestinal** motility, and **intestinal** conditions that cause the same. Such conditions include, but are not limited to, irritable **bowel** syndrome (IBS), infectious diseases of the small and large **intestines**, and symptoms of any of the foregoing. In particular, the present invention discloses methods of using (R)-verapamil, as well as compns. and formulations contg. the same.

IC ICM A61K031-277

INCL 514520000

CC 1-9 (Pharmacology)

Section cross-reference(s): 63

ST verapamil stereoisomer abnormal **gastrointestinal** motility therapy

IT Artery

(aorta; treatment of abnormal increases in **gastrointestinal** motility with verapamil)

IT Drug delivery systems

(beads; treatment of abnormal increases in **gastrointestinal** motility with verapamil)

IT Drug delivery systems

(buccal; treatment of abnormal increases in **gastrointestinal** motility with verapamil)

IT Drug delivery systems

(caplets; treatment of abnormal increases in **gastrointestinal** motility with verapamil)

IT Drug delivery systems

(capsules; treatment of abnormal increases in **gastrointestinal** motility with verapamil)

IT Intestine

(colon; treatment of abnormal increases in **gastrointestinal** motility with verapamil)

IT Granulation

(granulating agents; treatment of abnormal increases in **gastrointestinal** motility with verapamil)



- IT Drug delivery systems  
(granules; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Drug delivery systems  
(intravaginal; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Intestine, disease  
(irritable bowel syndrome; treatment of abnormal  
increases in gastrointestinal motility with verapamil)
- IT Intestine  
(large, infection; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Drug delivery systems  
(nasal; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Drug delivery systems  
(oral; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Drug delivery systems  
(osmotic pumps; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Drug delivery systems  
(parenterals; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Perfumes  
(perfuming agents; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Drug delivery systems  
(rectal; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Drug delivery systems  
(sachets; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Intestine, disease  
(small, infection; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Drug delivery systems  
(solids; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Drug delivery systems  
(sublingual; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Drug delivery systems  
(suppositories; treatment of abnormal increases in  
gastrointestinal motility with verapamil)
- IT Drug delivery systems  
(suspensions; treatment of abnormal increases in  
gastrointestinal motility with verapamil)

- IT Drug delivery systems  
(tablets, instant-release and modified-release; treatment of abnormal increases in **gastrointestinal** motility with verapamil)
- IT Drug delivery systems  
(topical; treatment of abnormal increases in **gastrointestinal** motility with verapamil)
- IT Antioxidants
- Binders
- Carriers
- Coating materials
- Coloring materials
- Crosslinking agents
- Emulsifying agents
- Flavoring materials
- Gastrointestinal** motility
- Gelation agents
- Human
- Humectants
- Lubricants
- Muscle contraction
- Plasticizers
- Preservatives
- Release coatings
- Setting agents
- Stabilizing agents
- Surfactants
- Sweetening agents
- Thickening agents
- Vas deferens
- Vasodilation
- Wetting agents  
(treatment of abnormal increases in **gastrointestinal** motility with verapamil)
- IT Carbohydrates, biological studies
- Polyesters, biological studies
- Polyoxyalkylenes, biological studies
- Polyurethanes, biological studies  
(treatment of abnormal increases in **gastrointestinal** motility with verapamil)
- IT Polymers, biological studies  
(water insol.; treatment of abnormal increases in **gastrointestinal** motility with verapamil)
- IT Polymers, biological studies  
(water-sol.; treatment of abnormal increases in **gastrointestinal** motility with verapamil)
- IT 9002-88-4, Poly(ethylene)  
(high and low d.; treatment of abnormal increases in

**gastrointestinal motility with verapamil)**  
IT 7361-61-7, Xylazine 10238-21-8, Glibenclamide 19216-56-9,  
Prazosin 38304-91-5, Minoxidil  
(treatment of abnormal increases in **gastrointestinal**  
motility with verapamil)  
IT 21829-25-4, Nifedipine 36622-29-4, (S)-Verapamil 38321-02-7,  
(R)-VERAPAMIL  
(treatment of abnormal increases in **gastrointestinal**  
motility with verapamil)  
IT 9002-86-2, Poly(vinyl chloride) 9003-20-7, Poly(vinylacetate)  
9003-21-8, Poly(methyl acrylate) 9003-42-3, Poly(ethyl  
methacrylate) 9003-44-5, Poly(vinyl isobutyl ether) 9003-63-8,  
Poly(butylmethacrylate) 9004-34-6, Cellulose, biological studies  
9004-35-7, Cellulose acetate 9004-36-8, Cellulose acetate butyrate  
9004-38-0, Cellulose acetate phthalate 9004-39-1, Cellulose  
acetate propionate 9004-48-2, Cellulose propionate 9004-57-3,  
Ethylcellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3,  
Hydroxypropylmethylcellulose 9004-67-5, Methylcellulose  
9005-25-8, Starch, biological studies 9011-14-7, Poly(methyl  
methacrylate) 9011-15-8, Poly(isobutyl methacrylate) 9012-09-3,  
Cellulose triacetate 25038-59-9, Poly(ethylene terephthalate),  
biological studies 25087-17-6, Poly(hexylmethacrylate)  
25189-01-9, Poly(phenylmethacrylate) 25322-68-3, Polyethylene  
glycol 25719-52-2, Poly(lauryl methacrylate) 25986-77-0,  
Poly(octadecylacrylate) 26124-32-3, Poly(isopropyl acrylate)  
26335-74-0, Poly(isobutylacrylate) 37200-12-7, Poly(isodecyl  
methacrylate)  
(treatment of abnormal increases in **gastrointestinal**  
motility with verapamil)

L21 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2003:334877 HCAPLUS  
DOCUMENT NUMBER: 138:343897  
TITLE: Gastric-retentive losartan dosage form for  
hypertension treatment  
INVENTOR(S): Devane, John; Cumming, K. Iain; Hou,  
Sui Yuen Eddie; Gusler, Gloria M.  
PATENT ASSIGNEE(S): Depomed, Inc., USA  
SOURCE: PCT Int. Appl., 31 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003035039

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,  
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,  
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,  
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,  
NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,  
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
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EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,  
TG

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US 2003158244

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US 2002-280852

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EP 1438027

A1

20040721

EP 2002-781664

200210  
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PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK  
JP 2005508358 T2 20050331 JP 2003-537606

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PRIORITY APPLN. INFO.:

US 2001-335247P P

200110  
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200210  
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AB A method of treatment for hypertension and other disease states  
comprises the delivery of losartan in a gastric-retentive dosage  
form. Thus tablets were obtained from losartan potassium 8.3, PEG  
25.0, HPMC 25.0, lactose monohydrate 40.7, and Mg stearate 1 mg.

IC ICM A61K009-20

ICS A61K031-415

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

IT Intestine

(duodenum; gastric-retentive losartan dosage form for  
hypertension treatment)

IT Intestine

(small; gastric-retentive losartan dosage form for hypertension treatment)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:518455 HCAPLUS

DOCUMENT NUMBER: 129:239401

TITLE: Assessment of regional differences in **intestinal** fluid movement in the rat using a modified in situ single pass perfusion model

AUTHOR(S): Raoof, Araz A.; Butler, Jackie; Devane, John G.

CORPORATE SOURCE: IVIVR Cooperative Working Group, Elan Pharmaceutical Technologies, Athlone, Ire.

SOURCE: Pharmaceutical Research (1998), 15(8), 1314-1316  
CODEN: PHREEB; ISSN: 0724-8741

PUBLISHER: Plenum Publishing Corp.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Transmucosal fluid movement was investigated in 3 different regions of the rat **intestine** (upper small **intestine**, lower small **intestine** and the large **intestine**) using a developed in situ single pass perfusion model automated to perfuse 12 rats simultaneously. <sup>14</sup>C-polyethylene glycol 4000 (<sup>14</sup>C-PEG) was used as an impermeable marker for measuring net water flux with antipyrine as a transcellular passively absorbed marker. Antipyrine is totally absorbed for the gut following oral administration and its **intestinal** absorption, using in situ single pass perfusion in rats, was shown to increase and decrease considerably with fluid absorption and secretion, resp. The variation in the **intestinal** fluid movement obsd. in this study did not affect regional absorption of the passively absorbed compd. antipyrine. The effect of such variation on the regional absorption of carrier mediated compds., nevertheless, remains unclear. The results are discussed in relation to the prediction of drug absorption after oral administration.

CC 1-1 (Pharmacology)

ST **intestine** fluid movement model drug absorption

IT **Intestine**

(assessment of regional differences in **intestinal** fluid movement in rat using a modified in situ single pass perfusion model)

IT Biological transport

(drug; assessment of regional differences in **intestinal** fluid movement in rat using a modified in situ single pass

perfusion model)  
IT Biological transport  
(uptake; assessment of regional differences in intestinal  
fluid movement in rat using a modified in situ single pass  
perfusion model)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L21 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:481723 HCAPLUS

DOCUMENT NUMBER: 129:235493

TITLE: What is the **gastrointestinal** transit  
of very small particles in humans?

AUTHOR(S): Brown, J.; Ramtoola, Z.; Cumming, I.; Butler,  
J.; Devane, J. G.; Wilding, I. R.

CORPORATE SOURCE: Pharmaceutical Profiles Limited, Nottingham, UK  
SOURCE: Proceedings of the International Symposium on  
Controlled Release of Bioactive Materials  
(1998), 25th, 126-127

CODEN: PCRMEY; ISSN: 1022-0178

PUBLISHER: Controlled Release Society, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The **gastrointestinal** transit properties of 3 very small  
formulations were comparable to those reported previously for  
conventional multiparticulate preps. which will be advantageous in  
their use for oral peptide and antigen delivery. In addn. the study  
offers a new strategy for the neutron activation radiolabeling of  
small particles using Sm acetylacetonate which significantly extends  
the versatility fo scintigraphy as applied to the oral route.

CC 63-5 (Pharmaceuticals)

ST oral microparticle **gastrointestinal** transit

IT Digestive tract

Particle size

Scintigraphy

(**gastrointestinal** transit of very small particles in  
humans)

IT Drug delivery systems

(microparticles, oral; **gastrointestinal** transit of very  
small particles in humans)

IT 14589-42-5, Samarium acetylacetonate

(**gastrointestinal** transit of very small particles in  
humans)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN  
THE RE FORMAT

L21 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:234304 HCAPLUS

DOCUMENT NUMBER: 128:261801

TITLE: A novel multiunit controlled-release system

AUTHOR(S): Butler, J.; Cumming, I.; Brown, J.; Wilding, I.;  
Devane, J. G.

CORPORATE SOURCE: Elan Pharmaceutical Technologies, Athlone, Ire.

SOURCE: Pharmaceutical Technology (1998), 22(3),  
122,124,126,128,130,132,134,138

CODEN: PTECDN; ISSN: 0147-8087

PUBLISHER: Advanstar Communications, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB PRODAS is a controlled-release system that combines the advantages of tablet-based technol. with presentation as a multiunit system, thus avoiding the potential problem of single-unit systems for complete dose failure or dose dumping. It also allows for customized delivery in terms of combinations of release rates and mechanisms as well as targeted release to different segments of the GI tract. This article describes a study that compared the GI transit of PRODAS with that of a traditional multiparticulate system under fasted and fed conditions using the noninvasive technique of .gamma.-scintigraphy. Transit characteristics of the multiunit formulation were similar to those of the multi-particulate formulation, indicating that the multiunit technol. achieved the same relative independence to GI transit characteristics as multiparticulate systems.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1

IT Intestine

(colon; multiunit controlled-release drug delivery system)

IT Intestine

(small; multiunit controlled-release drug delivery system)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L21 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:6895 HCAPLUS

DOCUMENT NUMBER: 128:123394

TITLE: Comparison of methodologies for evaluating  
regional intestinal permeabilityAUTHOR(S): Raoof, A.; Moriarty, D.; Brayden, D.; Corrigan,  
O. I.; Cumming, I.; Butler, J.; Devane,  
J.

CORPORATE SOURCE: Elan Corp. Plc, Athlone, Ire.

SOURCE: Advances in Experimental Medicine and Biology

(1997), 423(In Vitro-In Vivo Correlations),  
181-189

CODEN: AEMBAP; ISSN: 0065-2598

PUBLISHER: Plenum Publishing Corp.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors compared the permeability of a no. of drug candidates for inclusion in extended release products. The following 3 model systems were used: the in vitro vascularly perfused rat gut segment, the in situ (single pass) rat gut perfusion system and the Caco-2 cell monolayer system. In the two rat gut systems, three sep. sections of gut were investigated, the uppers mall **intestine**, the lower small **intestine** and the large intestine. In general, the compds. studied in the rat models were found to have a high permeability relative to marker compds. atenolol and antipyrine which are poor and high permeability marker compds., resp. The permeability trends obtained using the in vitro model were similar to those obtained using the in situ model, i.e., both sets of values were found to decrease distally from duodenum to **colon**. Due to differences, no correlation was established between the three different models.

CC 1-1 (Pharmacology)

Section cross-reference(s): 63

ST drug **intestine** permeability methodol

IT Animal cell line

(Caco-2; comparison of methodologies for evaluating regional **intestinal** permeability of drugs)

IT Drug bioavailability

Drug delivery systems

**Intestine**

Permeability

(comparison of methodologies for evaluating regional **intestinal** permeability of drugs)

IT Biological transport

(drug; comparison of methodologies for evaluating regional **intestinal** permeability of drugs)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L21 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:496048 HCAPLUS

DOCUMENT NUMBER: 122:298853

TITLE: The effect of food on the  
**gastrointestinal** transit and systemic  
absorption of naproxen from a novel  
sustained-release formulation

AUTHOR(S): Kenyon, C. J.; Hooper, G.; Tierney, D.; Butler,



J.; Devane, J.; Wilding, I. R.  
CORPORATE SOURCE: Pharmaceutical Profiles Limited, 2 Faraday  
Building, Highfields Science Park,  
Nottingham, NG7 2QP, NG7 2QP, UK  
SOURCE: Journal of Controlled Release (1995), 34(1),  
31-6  
CODEN: JCREEC; ISSN: 0168-3659  
PUBLISHER: Elsevier  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The in vivo behavior of a novel sustained-release formulation of  
naproxen was investigated using gamma scintigraphy in eight healthy  
male volunteers under fasted and fed conditions. Disintegration of  
the tablet into discrete sustained-release pellets occurred in the  
stomach shortly after administration. Feeding resulted in a lag  
time prior to the onset of gastric emptying but food did not affect  
transit through the small intestine. Post-prandial  
administration of the sustained-release formulation did not affect  
the disintegration of the tablet or the bioavailability of the drug.  
CC 63-5 (Pharmaceuticals)  
Section cross-reference(s): 1  
IT **Intestine**  
(small, food interaction with naproxen bioavailability from  
sustained-release tablets in humans)  
  
L21 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1992:476353 HCAPLUS  
DOCUMENT NUMBER: 117:76353  
TITLE: New developments in sustained-release  
antihypertensive therapy: formulation and  
pharmacokinetic considerations  
AUTHOR(S): Devane, John G.; Mulligan, Seamus;  
Kavanagh, M.; Davis, Stanley S.; Sparrow, Robert  
A.; Wilding, Ian R.  
CORPORATE SOURCE: Elan Pharm. Res. Corp., Gainesville, GA, USA  
SOURCE: American Journal of Cardiology (1992), 69(13),  
23E-27E  
CODEN: AJCDAG; ISSN: 0002-9149  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB In order to achieve a consistently absorbed form of nifedipine over  
24 h, a novel formulation approach, INDAS, was used to develop a  
once-daily, sustained-release (SR) form of nifedipine that could  
provide effective control of blood pressure at a low total daily  
dose. The pharmacokinetic characteristics of this new formulation  
of nifedipine-SR were compared with those of divided doses of  
conventional nifedipine. The SR formulation achieved a lower peak  
plasma nifedipine level but with a prolonged plasma profile

characterized by an extended time to peak plasma levels (Tmax), a higher trough plasma level, a longer apparent half-life, and a markedly lower peak-to-trough fluctuation in plasma nifedipine concns. In a sep. study, the **gastrointestinal** transit parameters and phys. characteristics of the SR tablet were evaluated. This study established that the large intestine is the major site of residence and absorption for this dosage form. The phys. erosion and disintegration characteristics of the SR formulation are such that a well-maintained absorption of nifedipine is consistently achieved over the 24-h dosing interval.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1

IT **Intestine**, metabolism

(large, nifedipine absorption by, from sustained-release tablets in humans, in antihypertensive therapy)

L21 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:412445 HCAPLUS

DOCUMENT NUMBER: 111:12445

TITLE: Pharmacokinetic properties and clinical efficacy of once-daily sustained-release naproxen

AUTHOR(S): Kelly, J. G.; Kinney, C. D.; Devane, J. G.; Mulligan, S.; Colgan, B. V.

CORPORATE SOURCE: Inst. Biopharm., Athlone, Ire.

SOURCE: European Journal of Clinical Pharmacology (1989), 36(4), 383-8

CODEN: EJCPAS; ISSN: 0031-6970

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The pharmacokinetics and clin. efficacy of a once-daily sustained-release formulation of naproxen (sodium salt) were compared with those of conventional-release agents. In a single-dose pharmacokinetic study, the rate of absorption of the sustained-release prepn. was less than that of a conventional-release prepn. but the extent of absorption was the same. As is the case with conventional-phase naproxen, food decreased the rate but not the extent of absorption of the sustained-release formulation. On multiple-dose administration for 7 days, the area under the concn.-time curve) and av. concns. of the sustained-release prepn. (1 g daily) were the same as those for conventional-release prepn. of naproxen sodium (250 mg 4 times daily) and naproxen free acid (500 mg daily). The conventional-release sodium salt was absorbed more quickly, with no differences in bioavailability. A double-blind clin. comparison in patients with osteoarthritis showed the sustained-release prepn. (1 g daily) to be equiv. in efficacy to conventional naproxen capsules (500 mg twice daily) but to give a lower incidence of **gastrointestinal** side-effects. The results suggest that

sustained-release naproxen sodium has potential for use as a once-daily treatment for inflammatory disease.

CC 63-5 (Pharmaceuticals)  
Section cross-reference(s): 1